Arthur, L.
08/976560

(FILE 'CAPLUS' ENTERED AT 14:00:35 ON 05 MAR 1999)

- key terms

=> d que

L1 1718 SEA FILE=CAPLUS ABB=ON PLU=ON (BIPOLAR? OR BI POLAR? OR AFFECTIVE) (S) (DISEAS? OR DISORDER)

L2 49 SEA FILE=CAPLUS ABB=ON PLU=ON (BAD OR BP) (S) (BIPOLAR? OR BI POLAR?)

L3 23 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR L2) AND CHROMOSOM? (1A) 18

L4 14 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND (MUTAT? OR MUTAGEN? OR MUTANT OR POLYMORPH? OR POLY MORPH?)

=> d 1-14 .beverly

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 1999 ACS

AN 1998:672566 CAPLUS

DN 129:286742

TI Fsh16 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders

SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2

IN Chen, Hong; Freimer, Nelson B.

APPLICATION NO.	DATE
WO 98-US6210	19980327
AU 98-67867	19980327

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842726	A1	19981001	WO 98-US6210	19980327
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9867867	A1	19981020	AU 98-67867	19980327

PY 1998
1998

AB The present invention relates to the mammalian fsh16 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh16 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh16 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh16 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh16 and to using such compds. as therapeutic agents in the treatment of fsh16 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh16 **disorders** and

neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:672564 CAPLUS
DN 129:271555
TI Fsh15w6 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
IN Chen, Hong; Freimer, Nelson B.

	APPLICATION NO.	DATE
AI	WO 98-US6211	19980327
	US 97-828007	19970327
	AU 98-67868	19980327

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9842724	A1	19981001	WO 98-US6211	19980327
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5866412	A	19990202	US 97-828007	19970327
AU 9867868	A1	19981020	AU 98-67868	19980327

PY 1998
1999
1998

AB The present invention relates to the mammalian fsh15w6 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh15w6 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh15w6 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh15w6 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh15w6 and to using such compds. as therapeutic agents in the treatment of fsh15w6 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh15w6 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of

these **disorders**.

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:672563 CAPLUS
DN 129:286740
TI Fsh22 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
IN Chen, Hong; Freimer, Nelson B.

	APPLICATION NO.	DATE
AI	WO 98-US6209	19980327
	AU 98-67866	19980327

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842723	A1	19981001	WO 98-US6209	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9867866	A1	19981020	AU 98-67866	19980327

PY 1998
1998
AB The present invention relates to the mammalian fsh22 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh22 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh22 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh22 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh22 and to using such compds. as therapeutic agents in the treatment of fsh22 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh22 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:672479 CAPLUS
DN 129:287565
TI Methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
SO PCT Int. Appl., 94 pp.

CODEN: PIXXD2

IN Chen, Hong; Freimer, Nelson B.

	APPLICATION NO.	DATE
AI	WO 98-US6208	19980327
	AU 98-67865	19980327

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842362	A1	19981001	WO 98-US6208	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9867865	A1	19981020	AU 98-67865	19980327

PY 1998
1998

AB The present invention relates to the mammalian fsh05 gene, a novel gene assocd. with **bipolar affective disorder (BAD)** in humans. The invention encompasses fsh05 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh05 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh05 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh05 and to using such compds. as therapeutic agents in the treatment of fsh05 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh05 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:582231 CAPLUS
DN 129:340353
TI No evidence for significant linkage between **bipolar affective disorder** and **chromosome 18** pericentromeric markers in a large series of multiplex extended pedigrees
SO Am. J. Hum. Genet. (1998), 62(4), 916-924
CODEN: AJHGAG; ISSN: 0002-9297
AU Knowles, James A.; Rao, Peter A.; Cox-Matise, Tara; Loth, Jo Ellen; De Jesus, Gracielle M.; Levine, Laura; Das, Kamna; Penchaszadeh, Graciela K.; Alexander, Joyce R.; Lerer, Bernard; Endicott, Jean; Ott, Jurg; Gilliam, T. Conrad; Baron, Miron
PY 1998

AB **Bipolar affective disorder** (BP) is a major neuropsychiatric **disorder** with high heritability and complex inheritance. Previously reported linkage between BP and DNA markers in the pericentromeric region of **chromosome 18**, with a parent-of-origin effect (linkage was present in pedigrees with paternal transmission and absent in pedigrees with exclusive maternal inheritance), has been a focus of interest in human genetics. We reexamd. the evidence in one of the largest samples reported to date (1013 genotyped individuals in 53 unilineal multiplex pedigrees), using 10 highly **polymorphic** markers and a range of parametric and nonparametric analyses. There was no evidence for significant linkage between BP and **chromosome 18** pericentromeric markers in the sample as a whole, nor was there evidence for significant parent-of-origin effect (pedigrees with paternal transmission were not differentially linked to the implicated chromosomal region). Two-point LOD scores and single-locus sib-pair results gave some support for suggestive linkage, but this was not substantiated by multilocus anal., and the results were further tempered by multiple test effects. We conclude that there is no compelling evidence for linkage between BP and **chromosome 18** pericentromeric markers in this sample.

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:293653 CAPLUS
DN 129:1406
TI Chromosomal markers and diagnostic tests for manic-depressive illness
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
IN Detera-Wadleigh, Sevilla D.; Gershon, Elliot S.; Badner, Judith A.; Goldin, Lynn R.; Berrettini, Wade H.; Yoshikawa, Takeo; Sanders, Alan R.; Esterling, Lisa E.

	APPLICATION NO.	DATE
AI	WO 97-US19381	19971028
	AU 98-51509	19971028

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9818963	A1	19980507	WO 97-US19381	19971028
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9851509 A1 19980522 AU 98-51509 19971028
PY 1998
1998
AB Methods and compns. are provided for detg. a genotype assocd. with increased susceptibility to manic-depressive illness. The genotype is detd. using markers for a region of **chromosome** 18 exhibiting linkage disequil. with manic-depressive illness. The invention also provides for a novel myo-inositol monophosphatase protein encoded for on **chromosome** **18**. Using direct cDNA selection and phys. mapping by PCR, 25 novel, **chromosome** **18**-specific cDNAs expressed in infant brain have been identified and positionally cataloged. A cDNA for a gene assocd. with manic-depression was identified. Based on sequence homol. and presence of protein motifs, the gene is proposed to encode myo-inositol monophosphatase. The promoter region of the gene was also isolated and sequenced.

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:162390 CAPLUS
DN 128:255702
TI Closing in on genes for manic-depressive illness and schizophrenia
SO Neuropsychopharmacology (1998), 18(4), 233-242
CODEN: NEROEW; ISSN: 0893-133X
AU Gershon, Elliot S.; Badner, Judith A.; Goldin, Lynn R.; Sanders, Alan R.; Cravchik, Anibal; Detera-Wadleigh, Sevilla D.
PY 1998
AB A review, with 64 refs. Advances in the human genetic map, and in genetic anal. of linkage and assocn. in complex inheritance traits, have led to genetic progress in the major psychoses. For chromosome 6 in schizophrenia, and **chromosomes** **18** and 21 in manic-depressive illness, there are reports of linkage in several independent data sets. These are small effect genes, best detected with affected-relative-pair linkage methods. Assocn. with candidate genes is an alternative strategy to uncovering susceptibility genes for these illnesses, but convincing assocns. remain to be demonstrated. New clin. and lab. investigation methods are being developed. Testing every gene in the human genome for assocn. with illness has recently been proposed. This would require further progress in characterizing the genome and in automated large-scale genotyping. The best type of pedigree sampling for common disease studies, whether for linkage or assocn., is not yet established. An endophenotype hybrid strategy can combine genetic linkage, assocn., and pathophysiol. studies. As clin. mol. investigation methods advance, identification of disease susceptibility **mutations** and delineation of their pathophysiol. roles may be expected.

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:29510 CAPLUS

DN 128:176630
TI Rapid cloning of expanded trinucleotide repeat sequences from genomic DNA
SO Nat. Genet. (1998), 18(1), 72-75
CODEN: NGENEC; ISSN: 1061-4036
AU Koob, Michael D.; Benzow, Kellie A.; Bird, Thomas D.; Day, John W.; Moseley, Melinda L.; Ranum, Laura P. W.
PY 1998
AB Trinucleotide repeat expansions have been shown to cause a no. of neurodegenerative diseases. A hallmark of most of these diseases is the presence of anticipation, a decrease in the age at onset in consecutive generations due to the tendency of the unstable trinucleotide repeat to lengthen when passed from one generation to the next. The involvement of trinucleotide repeat expansions in a no. of other **diseases** - including familial spastic paraplegia, schizophrenia, **bipolar affective disorder** and spinocerebellar ataxia type 7 (SCA7) - is suggested both by the presence of anticipation and by repeat expansion detection (RED) anal. of genomic DNA samples. The involvement of trinucleotide expansions in these diseases, however, can be conclusively confirmed only by the isolation of the expansions present in these populations and detailed anal. to assess each expansion as a possible pathogenic **mutation**. We describe a novel procedure for quick isolation of expanded trinucleotide repeats and the corresponding flanking nucleotide sequence directly from small amts. of genomic DNA by a process of Repeat Anal., Pooler Isolation and Detection of individual clones contg. expanded trinucleotide repeats (RAPID cloning). We have used this technique to clone the pathogenic SCA7 CAG expansion from an archived DNA sample of an individual affected with ataxia and retinal degeneration.

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1997:679203 CAPLUS
DN 127:327441
TI Methods for detecting **bipolar** mood **disorder** susceptibility locus on human chromosome 18q
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
IN Friemer, Nelson B.; Leon, Pedro; Reus, Victor I.; Sandkuijl, Lodewijk A.; Barondes, Samuel H.

	APPLICATION NO.	DATE
AI	WO 97-US4904	19970327
	AU 97-24238	19970327
	WO 97-US14892	19970822
	AU 97-41604	19970822

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Searcher : Shears 308-4994

PI WO 9737043 A1 19971009 WO 97-US4904 19970327
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9724238 A1 19971022 AU 97-24238 19970327
WO 9807887 A1 19980226 WO 97-US14892 19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9741604 A1 19980306 AU 97-41604 19970822
PY 1997
1997
1998
1998

AB The present invention is directed to methods of detecting the presence of a **bipolar** mood **disorder** susceptibility locus in an individual, comprising analyzing a sample of DNA for the presence of a DNA **polymorphism** on the long arm of **chromosome 18** between markers D18S469 and D18S554, wherein the DNA **polymorphism** is assocd. with a form of **bipolar** mood **disorder (BP)**. The invention for the first time provides strong evidence of a susceptibility gene for BP that is located in the 18q22-q23 region of the long arm of **chromosome 18**. The disclosure describes the use of linkage anal. and genetic markers in the 18q22-q23 region to fine map the region and the use of genetic markers to genetically diagnose (genotype) BP in individuals, to confirm phenotypic diagnoses of BP, to det. appropriate treatments for patients with particular genotypic subtypes. Isolated polynucleotides useful for genetic linkage anal. of BP-I and methods for obtaining such isolated polynucleotides are also described. In screening for a BP susceptibility locus, only those individuals with the most severe and clin. distinctive form of BP were considered as affected. Two large pedigrees were selected from a genetically homogeneous population, that of the Central Valley of Costa Rica. The entire human genome was screened for linkage using mapped microsatellite markers and a model for genetic anal. in which most of the linkage information derived from affected individuals. Three

lines of evidence supported the localization of a BP susceptibility locus to 18q22-q23: assocn. anal., linkage anal., and direct observation of a conserved marker haplotype.

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1997:675831 CAPLUS
DN 128:842
TI A novel, heritable, expanding CTG repeat in an intron of the SEF2-1 gene on chromosome 18q21.1
SO Hum. Mol. Genet. (1997), 6(11), 1855-1863
CODEN: HMGEE5; ISSN: 0964-6906
AU Breschel, T. S.; McInnis, M. G.; Margolis, R. L.; Sirugo, G.; Corneliussen, B.; Simpson, S. G.; McMahon, F. J.; MacKinnon, D. F.; Xu, J. F.; Pleasant, N.; Huo, Y.; Ashworth, R. G.; Grundstrom, C.; Grundstrom, T.; Kidd, K. K.; DePaulo, J. R.; Ross, C. A.
PY 1997
AB There are currently 13 diseases known to be caused by unstable triplet repeat **mutations**; however, there are some instances (as with FRAXF and FRA16) when these **mutations** appear to be asymptomatic. In a search for **polymorphic** CTG repeats as candidate genes for **bipolar disorder**, we screened a genomic human **chromosome 18**-specific library and identified a 1.6 kb clone (7,6A) with a CTG24 repeat that maps to 18q21.1. The CTG repeat locus, termed CTG18.1, is located within an intron of human SEF2-1, a gene encoding a basic helix-loop-helix DNA binding protein involved in transcriptional regulation. The CTGn repeat is highly **polymorphic** and very enlarged alleles, consistent with expansions of up to CTG2100, were identified. PCR and Southern blot anal. in pedigrees ascertained for a Johns Hopkins University **bipolar disorder** linkage study and in CEPH ref. pedigrees revealed a tripartite distribution of CTG18.1 alleles with stable alleles (CTG10-CTG37), moderately enlarged and unstable alleles (CTG53-CTG250), and very enlarged, unstable alleles (CTG800-CTG2100). Moderately enlarged alleles were not assocd. with an abnormal phenotype and have a combined enlarged allele frequency of 3% in the CEPH and bipolar populations. Very enlarged alleles, detectable only by Southern blot anal. of genomic digests, have thus far been found in only three individuals from our bipolar pedigrees, and to date, have not been found in any of the CEPH ref. pedigrees. These enlarged alleles may arise, at least in part, via somatic **mutation**.

L4 ANSWER 11 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1997:673386 CAPLUS
DN 128:10756
TI Genomic structure and chromosomal localization of a human myo-inositol monophosphatase gene (IMPA)
SO Genomics (1997), 45(1), 113-122

CODEN: GNMCEP; ISSN: 0888-7543

AU Sjoholt, Gry; Molven, Anders; Lovlie, Roger; Wilcox, Andrea; Sikela, James M.; Steen, Vidar M.

PY 1997

AB Manic-depressive illness is a serious psychiatric disorder that in many, but far from all, patients can be treated with lithium. The main causes for discontinuation of lithium therapy are unpleasant or serious side effects and lack of response. The reason for the striking variation in clin. efficacy of lithium treatment among bipolar patients is not known. The enzyme myo-inositol monophosphatase (IMPase) has been postulated as a target for the mood-stabilizing effects of lithium, but variation in the coding region of the human IMPA gene encoding IMPase activity has not been obsd. in manic-depressive patients (Steen et al., Pharmacogenetics, 1996, 6, 113-116). It is nevertheless conceivable that **polymorphisms** or **mutations** in the noncoding regions of this gene could influence the lithium response in psychiatric patients. As a first step in investigating this possibility, we here report the genomic structure of the human IMPA gene. The gene is composed of at least nine exons and covers more than 20 kb of sequence on chromosome 8q21.13-q21.3. In the 3'-untranslated part of the gene, we obsd. a **polymorphism** (a G to A transition) and also two short sequences similar to the inositol/cholin-responsive element consensus. Finally, we postulate that two addnl. IMPA-like transcripts originate from the human genome, one from a position close to IMPA itself on chromosome 8 and the other from chromosome 18p. Our data may contribute to the identification of genetic factors involved in the pathogenesis and detn. of treatment response in manic-depressive illness.

L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 1999 ACS

AN 1996:305712 CAPLUS

DN 125:2629

TI Analysis of **chromosome 18** DNA markers in multiplex pedigrees with manic depression

SO Biol. Psychiatry (1996), 39(8), 689-696
CODEN: BIPCBF; ISSN: 0006-3223

AU Coon, Hilary; Hoff, M.; Holik, J.; Hadley, D.; Fang, N.; Reimherr, F.; Wender, P.; Byerley, William

PY 1996

AB Six pedigrees segregating manic-depressive illness (MDI) were analyzed for linkage to 21 highly **polymorphic** microsatellite DNA markers on **chromosome 18**. These markers span almost the entire length of the chromosome, and gaps between markers are less than 20 cM. In particular, we analyzed several markers localizing to the pericentromeric region of **chromosome 18** which generated lod scores suggestive of linkage in an independent study. Lod score anal. was performed and results were examd. by family. One region produced

pos. lod scores, though at 18q23 and not in the pericentromeric region. We addnl. used two nonparametric methods because the true mode of transmission of MDI is unknown; results were again somewhat suggestive for markers in the region of 18q23 but not in the pericentromeric region.

L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1996:305711 CAPLUS
DN 124:334471
TI Linkage analysis of families with bipolar illness and **chromosome 18** markers
SO Biol. Psychiatry (1996), 39(8), 679-688
CODEN: BIPCBF; ISSN: 0006-3223
AU De bruyn, An; Souery, Daniel; Mendelbaum, Karine; Mendlewicz, Julien; Van Broeckhoven, Christine
PY 1996
AB Linkage of **bipolar** (**BP**) illness with **chromosome 18** markers located at 18p11 was recently reported. A possible role for **chromosome 18** in the etiol. of BP illness was implicated previously by the finding in three unrelated patients of a ring chromosome with breakpoints and deleted segments at 18pter-p11 and 18q23-qter. To test the potential importance of a gene defect on **chromosome 18** in our material, we examd. linkage with **chromosome 18** markers in two families with multiple patients with BP illness or BP spectrum disorders. Fourteen simple tandem repeat **polymorphisms** were used located in the chromosomal region 18p11 to 18q23 and sepd. by distances of approx. 10 cM on the genetic map. In one family linkage to **chromosome 18** could not be excluded. Linkage and segregation anal. in the family suggests that the 12-cM region between D18S51 and D18S61 located at 18q21.33-q23 may contain a candidate gene for BP illness.

L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1996:41004 CAPLUS
DN 124:108441
TI Evidence for linkage of **bipolar disorder** to **chromosome 18** with a parent-of-origin effect
SO Am. J. Hum. Genet. (1995), 57(6), 1384-94
CODEN: AJHGAG; ISSN: 0002-9297
AU Stine, O. Colin; Xu, Jianfeng; Koskela, Rebecca; McMahon, Francis J.; Gschwend, Michele; Friddle, Carl; Clark, Chris D.; Mclnnis, Melvin G.; Simpson, Sylvia G.; et al.
PY 1995
AB A susceptibility gene on **chromosome 18** and a parent-of-origin effect have been suggested for **bipolar affective disorder** (BPAD). We have studied 28 nuclear families selected for apparent unilinear transmission of the

BPAD phenotype, by using 31 **polymorphic** markers spanning **chromosome 18**. Evidence for linkage was tested with affected-sib-pair and LOD score methods under two definitions of the affected phenotype. The affected-sib-pair analyses indicated excess allele sharing for makers on 18p within the region reported previously. The greatest sharing was at D18S37: 64% in bipolar and recurrent unipolar (RUP) sib pairs (P = .0006). In addn., excess sharing of the paternally, but not maternally, transmitted alleles was obsd. at three markers on 18q: at D18S41, 51 bipolar and RUP sib pairs were concordant for paternally transmitted alleles, and 21 pairs were discordant (P = .0004). The evidence for linkage to loci on both 18p and 18q was strongest in the 11 paternal pedigrees, i.e., those in which the father or one of the father's sibs is affected. In these pedigrees, the greatest allele sharing (81%; P = .00002) and the highest LOD score (3.51; .THETA. = 0.0) were obsd. at D18S41. Our results provide further support for linkage of BPAD to **chromosome 18** and the first mol. evidence for a parent-of-origin effect operating in this disorder. The no. of loci involved, and their precise location, require further study.

(FILE 'CAPLUS' ENTERED AT 14:00:35 ON 05 MAR 1999)
L5 3 S BPI(S)(BIPOLAR? OR BI POLAR?)
L6 3 S L5 NOT L4
L7 2 S L6 AND CHROMOSOM?(1A)18
L8 0 S L7 AND (MUTAT? OR MUTAGEN? OR MUTANT OR POLYMORPH? OR POLY MORPH?)

=> d l7 1-2 .beverly

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1996:312108 CAPLUS
DN 125:2666
TI Genetic mapping using haplotype, association and linkage methods suggests a locus for severe **bipolar** disorder (**BPI**) at 18q22-q23
SO Nat. Genet. (1996), 12(4), 436-441
CODEN: NGENEC; ISSN: 1061-4036
AU Freimer, Nelson B.; Reus, Victor I.; Escamilla, Michael A.; McInnes, L. Alison; Spesny, Mitzi; Leon, Pedro; Service, Susan K.; Smith, Lauren B.; Silva, Sandra; et al.
PY 1996
AB Manic-depressive illness, or bipolar disorder (BP), is characterized by episodes of elevated mood (mania) and depression1. We designed a multistage study in the genetically isolated population of the Central Valley of Costa Rica2,3 to identify genes that promote susceptibility to severe BP (termed BPI), and screened the genome of two Costa Rican BPI pedigrees (McInnes et al., submitted). We considered only individuals who fulfilled very stringent diagnostic criteria for BPI to be affected. The strongest evidence for a BPI locus was obsd. in 18q22-q23. We tested 16 addnl. markers in this region and seven yielded peak lod scores over 1.0. These suggestive lod scores were obtained over a far greater chromosomal length (about 40 cM) than in any other genome region. This localization is supported by marker haplotypes shared by 23 of 26 BPI affected individuals studied. Addnl., marker allele frequencies over portions of this region are significantly different in the patient sample from those of the general Costa Rican population. Finally, we performed an anal. which made use of both the evidence for linkage and for assocn. in 18q23, and we obsd. significant lod scores for two markers in this region.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1996:312107 CAPLUS
DN 125:2665
TI A genome-wide search for chromosomal loci linked to bipolar affective disorder in the Old Order Amish
SO Nat. Genet. (1996), 12(4), 431-435
CODEN: NGENEC; ISSN: 1061-4036
AU Ginns, Edward I.; Ott, Jurg; Egeland, Janice A.; Allen, Cleona R.; Fann, Cathy S. J.; Pauls, David L.; Weissenbach, Jean; Carulli, John

P.; Falls, Kathleen M.; et al.
PY 1996
AB The most characteristic features of **bipolar** affective disorder (manic-depressive illness) are episodes of mania (**bipolar** I, **BPI**) or hypomania (**bipolar** II, BPII) interspersed with periods of depression. Manic-depressive illness afflicts about one percent of the population, and if untreated, is assocd. with an approx. 20% risk of suicide. Twin, family and adoption studies provide compelling evidence for a partial genetic etiol., but the mode(s) of inheritance has not been identified. Nonetheless, the majority of genetic linkage studies have assumed classical mendelian inheritance attributable to a single major gene. Although segregation analyses have yielded inconsistent results (with most studies rejecting a single locus inheritance model), the best single gene model is dominant inheritance if only BPI is considered. Reported linkages of bipolar affective disorder on **chromosomes** 11, **18**, 21 and X have been difficult to substantiate, and addnl. studies are required for replication or exclusion of these regions. We now present the results of our genome-wide linkage analyses that provide evidence that regions on chromosomes 6, 13 and 15 harbor susceptibility loci for bipolar affective disorder, suggesting that bipolar affective disorder in the Old Order Amish is inherited as a complex trait.

=> d his l9- ful; d 1-24 bib abs

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT' ENTERED AT 14:08:47 ON 05 MAR 1999)
L9 289 SEA ABB=ON PLU=ON (L1 OR L2 OR L5) AND CHROMOSOM?(1A) 18
L10 58 SEA ABB=ON PLU=ON L9 AND (MUTAT? OR MUTAGEN? OR MUTANT OR POLYMORPH? OR POLY MORPH?)
L11 24 DUP REM L10 (34 DUPLICATES REMOVED)

L11 ANSWER 1 OF 24 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 99-02055 BIOTECHDS
TI New isolated human fsh16 gene; protein and antibody used for neuropsychiatric condition diagnosis, therapy and drug screening, and to identify fsh16 gene **polymorphism**
AU Chen H; Freimer N B
PA Millennium-Pharm.; Univ.California
LO Cambridge, MA, USA; Oakland, CA, USA.
PI WO 9842726 1 Oct 1998
AI WO 98-US6210 27 Mar 1998
PRAI US 97-828009 27 Mar 1997
DT Patent
LA English

OS WPI: 99-045133 [04]
AN 99-02055 BIOTECHDS
AB A nucleic acid (NA, I) with a given 1,086 **bp** sequence that encodes a given 110 amino acid fsh16 protein sequence, or a NA encoding a protein with a protein sequence encoded by the NA deposited under ATCC 98349, is claimed. Also claimed is a NA that hybridizes to the complement of (I), and encodes a protein involved in neuropsychiatric **disorders**, as well as a NA that hybridizes to the complement of (I) under stringent conditions. The claims also cover a vector containing (I), a host cell transformed by that vector, a protein produced by the vector, and an antibody that specifically binds to the protein. These can be used to treat neuropsychiatric **disorders**, by modulating the activity or expression of the fsh16 gene or gene product. They can also be used to map the human chromosome 18q region between markers DS18S1121 and DS18S830, to detect **polymorphisms** in that region. This is of use in the diagnosis and treatment of neuropsychiatric **disorders** such as schizophrenia, attention deficit **disorder, bipolar affective disorder**, etc. They can also be used in drug screening to identify compounds useful in neurodegenerative **disorders**. (90pp)

DUPLICATE 1

L11 ANSWER 2 OF 24 MEDLINE
AN 1998198351 MEDLINE
DN 98198351
TI No evidence for significant linkage between **bipolar affective disorder** and **chromosome 18** pericentromeric markers in a large series of multiplex extended pedigrees.
AU Knowles J A; Rao P A; Cox-Matise T; Loth J E; de Jesus G M; Levine L; Das K; Penchaszadeh G K; Alexander J R; Lerer B; Endicott J; Ott J; Gilliam T C; Baron M
CS Columbia University College of Physicians and Surgeons and New York State Phychiatric Institute, New York, NY 10032, USA.
NC MH42535 (NIMH)
MH43979 (NIMH)
MH44292 (NIMH)
+
SO AMERICAN JOURNAL OF HUMAN GENETICS, (1998 Apr) 62 (4) 916-24.
Journal code: 3IM. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
EW 19980802
AB **Bipolar affective disorder** (**BP**) is a major neuropsychiatric **disorder** with high

heritability and complex inheritance. Previously reported linkage between **BP** and DNA markers in the pericentromeric region of **chromosome 18**, with a parent-of-origin effect (linkage was present in pedigrees with paternal transmission and absent in pedigrees with exclusive maternal inheritance), has been a focus of interest in human genetics. We reexamined the evidence in one of the largest samples reported to date (1,013 genotyped individuals in 53 unilineal multiplex pedigrees), using 10 highly **polymorphic** markers and a range of parametric and nonparametric analyses. There was no evidence for significant linkage between **BP** and **chromosome 18** pericentromeric markers in the sample as a whole, nor was there evidence for significant parent-of-origin effect (pedigrees with paternal transmission were not differentially linked to the implicated chromosomal region). Two-point LOD scores and single-locus sib-pair results gave some support for suggestive linkage, but this was not substantiated by multilocus analysis, and the results were further tempered by multiple test effects. We conclude that there is no compelling evidence for linkage between **BP** and **chromosome 18** pericentromeric markers in this sample.

L11 ANSWER 3 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1999:5859 SCISEARCH
GA The Genuine Article (R) Number: 147RM
TI Human G(olf) gene **polymorphisms** and vulnerability to **bipolar disorder**
AU Berrettini W H (Reprint); Vuoristo J; Ferraro T N; Buono R J; Wildenauer D; AlaKokko L
CS UNIV PENN, DEPT PSYCHIAT, PHILADELPHIA, PA 19104; UNIV PENN, DEPT GENET, PHILADELPHIA, PA 19104; UNIV OULU, DEPT MED BIOCHEM, COLLAGEN RES UNIT, OULU, FINLAND; UNIV BONN, DEPT PSYCHIAT, D-5300 BONN, GERMANY
CYA USA; FINLAND; GERMANY
SO PSYCHIATRIC GENETICS, (WIN 1998) Vol. 8, No. 4, pp. 235-238.
Publisher: RAPID SCIENCE PUBLISHERS, 2-6 BOUNDARY ROW, LONDON SE1 8NH, ENGLAND.
ISSN: 0955-8829.
DT Article; Journal
LA English
REC Reference Count: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Two intronic **polymorphisms** of the human alpha subunit of the olfactory G-protein (G(olf)) are described. They were detected with single-stranded conformational **polymorphism** (SSCP) methods and confirmed by sequencing both strands. These single base pair (bp) substitutions occur in introns 3 tan A/G at 35 bp 3' from the exon 3/intron 3 5' splice site) and 10 tan T/G at 7 bp 5' from the 3' splice site). Both **polymorphisms** are

relatively common, with minor allele frequencies of 31% (intron 3) and 16% (intron 10). The intron 3 variant shows no linkage disequilibrium with an intron 5 (CA)n microsatellite located approximately 50 kb 3' from the intron 3 variant, among a small group of German individuals with schizophrenia. The intron 3 variant is interesting because it may create an 'in-frame' cryptic splice site which, if activated, would add 12 residues to exon 3. The intron 10 variant is interesting because a purine is substituted for a pyrimidine in the 'polypyrimidine' tract of the 3' splice site, a single base substitution of the type which has been associated with aberrant splicing in the androgen receptor gene. Psychiatr Genet 8:235-238 (C) 1998 Lippincott Williams & Wilkins.

DUPLICATE 2

L11 ANSWER 4 OF 24 MEDLINE
AN 1998170231 MEDLINE
DN 98170231
TI Closing in on genes for manic-depressive illness and schizophrenia.
AU Gershon E S; Badner J A; Goldin L R; Sanders A R; Cravchik A; Detera-Wadleigh S D
CS Neurogenetics Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892-1274, USA.
SO NEUROPSYCHOPHARMACOLOGY, (1998 Apr) 18 (4) 233-42. Ref: 62
Journal code: ADQ. ISSN: 0893-133X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199807
EW 19980701
AB Advances in the human genetic map, and in genetic analysis of linkage and association in complex inheritance traits, have led to genetic progress in the major psychoses. For chromosome 6 in schizophrenia, and **chromosomes** 18 and 21 in manic-depressive illness, there are reports of linkage in several independent data sets. These are small effect genes, best detected with affected-relative-pair linkage methods. Association with candidate genes is an alternative strategy to uncovering susceptibility genes for these illnesses, but convincing associations remain to be demonstrated. New clinical and laboratory investigation methods are being developed. Testing every gene in the human genome for association with illness has recently been proposed (Risch and Merikangas 1996). This would require further progress in characterizing the genome and in automated large-scale genotyping. The best type of pedigree sampling for common disease studies, whether for linkage or association, is not yet established. An endophenotype hybrid strategy can combine genetic linkage, association, and pathophysiologic studies. As clinical molecular

investigation methods advance, identification of disease susceptibility **mutations** and delineation of their pathophysiological roles may be expected.

L11 ANSWER 5 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:946197 SCISEARCH
GA The Genuine Article (R) Number: 146HC
TI Failure to demonstrate parent-of-origin effect in transmission of **bipolar** II **disorder**
AU Kato T (Reprint); Winokur G; Coryell W; Rice J; Endicott J; Keller M B; Akiskal H S
CS UNIV TOKYO, FAC MED, DEPT PSYCHIAT, BUNKYO KU, HONGO 7-3-1, TOKYO 113, JAPAN (Reprint); UNIV IOWA, COLL MED, DEPT PSYCHIAT, IOWA CITY, IA 52242; SHIGA UNIV MED SCI, DEPT PSYCHIAT, OTSU, SHIGA 52021, JAPAN; WASHINGTON UNIV, DEPT PSYCHIAT, ST LOUIS, MO 63110; NEW YORK STATE PSYCHIAT INST & HOSP, NEW YORK, NY 10032; BROWN UNIV, BUTLER HOSP, PROVIDENCE, RI 02906; UNIV CALIF SAN DIEGO, SAN DIEGO, CA 91261
CYA JAPAN; USA
SO JOURNAL OF AFFECTIVE DISORDERS, (SEP 1998) Vol. 50, No. 2-3, pp. 135-141.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0165-0327.
DT Article; Journal
FS LIFE; SOCSEARCH
LA English
REC Reference Count: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Parent-of-origin effect (POE) is suggested in transmission of **bipolar disorder.** **Bipolar** II **disorder** (BPII) should be considered separately. Methods: The gender difference of transmitting parents, prevalence rate in children, and age at onset of patients in relation to the sex of the transmitting parent, were examined in 220 BPII patients. Results: No evidence suggesting involvement of POE was found. Conclusion: POE is not involved in transmission of BPII. Limitation: Number of subjects is not sufficient. Rate of interviewed subjects differs between mothers and fathers. Clinical relevance: Female BPII patients do not transmit the **disease** more often than male patients. (C) 1998 Elsevier Science B.V. All rights reserved.

L11 ANSWER 6 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:240447 SCISEARCH
GA The Genuine Article (R) Number: ZC526
TI A functional variant of the serotonin transporter gene in families with **bipolar affective disorder**
AU Ewald H (Reprint); Flint T; Degn B; Mors O; Kruse T A

CS INST BASIC PSYCHIAT RES, DEPT PSYCHIAT DEMOG, SKOVAGERVEJ 2, DK-8240 RISSKOV, DENMARK (Reprint); INST BASIC PSYCHIAT RES, DEPT BIOL PSYCHIAT, DK-8240 RISSKOV, DENMARK; AARHUS UNIV, INST HUMAN GENET, DK-8000 AARHUS, DENMARK
CYA DENMARK
SO JOURNAL OF AFFECTIVE DISORDERS, (MAR 1998) Vol. 48, No. 2-3, pp. 135-144.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0165-0327.
DT Article; Journal
FS LIFE; SOCSEARCH
LA English
REC Reference Count: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: The serotonin transporter protein (SERT) reuptakes serotonin from synapses and has been implied as the site of therapeutic action of many antidepressant drugs. SERT is one of the most relevant candidate genes for **bipolar affective disorder**. Recently a functionally important 44 basepair deletion in the regulatory region of the SERT gene was described. Association between this variant and **affective disorder** has been suggested. Methods: The present study analysed this variation and another variation in the SERT gene and nearby DNA markers in order to test for linkage between SERT and **bipolar affective disorder** in two Danish families. Results and conclusion: There was no evidence that variants in the SERT gene were a stronger dominant **disease** gene for the development of **affective disorder** in the families. The possibility of a recessive **disease** gene at or near SERT could not be excluded. Limitations: The present study cannot exclude if variations at or near the SERT gene were weak susceptibility genes or determine if they are important for other characteristics than presence or absence of **disease**. Clinical relevance: Further studies of the SERT gene in **affective** and other **disorders**, as well as in relation to treatment response to antidepressants are needed. (C) 1998 Elsevier Science B.V.

L11 ANSWER 7 OF 24 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-00993 BIOTECHDS
TI Medical methods relating to **bipolar** mood **disorder**; genotype analysis for use in diagnosis
AU Friemer N B; Leon P; Reus V I; Sandkuijl L A; Barondes S H
PA Univ.California
LO Oakland, CA, USA.
PI WO 9737043 9 Oct 1997
AI WO 97-US4904 27 Mar 1997

PRAI US 96-23438 23 Aug 1996; US 96-14498 29 Mar 1996
DT Patent
LA English
OS WPI: 97-535448 [49]
AN 98-00993 BIOTECHDS
AB A new method of predicting a Spanish or Amerindian patients likelihood of developing **bipolar** mood **disorder** involves determining the patient's genotype in a region on the long arm of **chromosome-18** by determining allele sizes at markers between D18S469 and D18S554, and comparing the genotype to genotypes of affected individuals. The analysis may also involve analyzing DNA of the patient's family members. Also claimed is a method of predicting a patients responsivity to drug treatment for **bipolar** mood **disorder**. Knowledge of the genotype at this locus may help in selecting appropriate treatments for the **disorder**. The markers are preferably located between markers D18S1121 and D18S380. The DNA **polymorphism** is located between D18S469 and D18S1161, D18S1161 and D18S1121, D18S1121 and D18S1009, D18S1109 and D18S380, D18S380 and D18S554, or D18S1009 and D18S554. (52pp)

DUPLICATE 4

L11 ANSWER 8 OF 24 MEDLINE
AN 1998027057 MEDLINE
DN 98027057
TI A novel, heritable, expanding CTG repeat in an intron of the SEF2-1 gene on chromosome 18q21.1.
AU Breschel T S; McInnis M G; Margolis R L; Sirugo G; Corneliussen B; Simpson S G; McMahon F J; MacKinnon D F; Xu J F; Pleasant N; Huo Y; Ashworth R G; Grundstrom C; Grundstrom T; Kidd K K; DePaulo J R; Ross C A
CS George Browne Genetics Laboratory, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
NC MH01088 (NIMH)
MH54701 (NIMH)
MH50763 (NIMH)
+
SO HUMAN MOLECULAR GENETICS, (1997 Oct) 6 (11) 1855-63.
Journal code: BRC. ISSN: 0964-6906.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U75701
EM 199803
AB There are currently 13 **diseases** known to be caused by unstable triplet repeat **mutations**; however, there are some instances (as with FRAXF and FRA16) when these **mutations** appear to be asymptomatic. In a search for **polymorphic** CTG

repeats as candidate genes for **bipolar disorder**, we screened a genomic human **chromosome 18** -specific library and identified a 1.6 kb clone (7,6A) with a CTG24 repeat that maps to 18q21.1. The CTG repeat locus, termed CTG18.1, is located within an intron of human SEF2-1, a gene encoding a basic hellx-loop-hellx DNA binding protein involved in transcriptional regulation. The CTGn repeat is highly **polymorphic** and very enlarged alleles, consistent with expansions of up to CTG2100, were identified. PCR and Southern blot analysis in pedigrees ascertained for a Johns Hopkins University **bipolar disorder** linkage study and in CEPH reference pedigrees revealed a tripartite distribution of CTG18.1 alleles with stable alleles (CTG10-CTG37), moderately enlarged and unstable alleles (CTG53-CTG250), and very enlarged, unstable alleles (CTG800-CTG2100). Moderately enlarged alleles were not associated with an abnormal phenotype and have a combined enlarged allele frequency of 3% in the CEPH and **bipolar** populations. Very enlarged alleles, detectable only by Southern blot analysis of genomic digests, have thus far been found in only three individuals from our **bipolar** pedigrees, and to date, have not been found in any of the CEPH reference pedigrees. These enlarged alleles may arise, at least in part, via somatic **mutation**.

L11 ANSWER 9 OF 24 MEDLINE DUPLICATE 5
AN 1998153638 MEDLINE
DN 98153638
TI Linkage of **bipolar affective disorder** to **chromosome 18** markers in a new pedigree series.
AU McMahon F J; Hopkins P J; Xu J; McInnis M G; Shaw S; Cardon L; Simpson S G; MacKinnon D F; Stine O C; Sherrington R; Meyers D A; DePaulo J R
CS Johns Hopkins University School of Medicine, Baltimore, MD, USA.. fmcm@welchlink.welch.jhu.edu
SO AMERICAN JOURNAL OF HUMAN GENETICS, (1997 Dec) 61 (6) 1397-404. Journal code: 3IM. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY)
LA English
FS Priority Journals
EM 199805
EW 19980503
AB Several groups have reported evidence suggesting linkage of **bipolar affective disorder** (BPAD) to **chromosome 18**. We have reported data from 28 pedigrees that showed linkage to marker loci on 18p and to loci 40 cM distant on 18q. Most of the linkage evidence derived from families with affected phenotypes in only the paternal lineage and

from marker alleles transmitted on the paternal chromosome. We now report results from a series of 30 new pedigrees (259 individuals) genotyped for 13 **polymorphic** markers spanning **chromosome 18**. Subjects were interviewed by a psychiatrist and were diagnosed by highly reliable methods. Genotypes were generated with automated technology and were scored blind to phenotype. Affected sib pairs showed excess allele sharing at the 18q markers D18S541 and D18S38. A parent-of-origin effect was observed, but it was not consistently paternal. No robust evidence of linkage was detected for markers elsewhere on **chromosome 18**. Multipoint nonparametric linkage analysis in the new sample combined with the original sample of families supports linkage on chromosome 18q, but the susceptibility gene is not well localized.

L11 ANSWER 10 OF 24 MEDLINE DUPLICATE 6
AN 1998060617 MEDLINE
DN 98060617
TI An integrated physical map of 18p11.2: a susceptibility region for **bipolar disorder.**
AU Esterling L E; Cox Matise T; Sanders A R; Yoshikawa T; Overhauser J; Gershon E S; Moskowitz M T; Detera-Wadleigh S D
CS Laboratory of Molecular Genetics, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, MD 20892, USA.. lesterlg@pop.nidcd.nih.gov
NC MH44292 (NIMH)
HG00151 (NHGRI)
SO MOLECULAR PSYCHIATRY, (1997 Oct-Nov) 2 (6) 501-4.
Journal code: CUM. ISSN: 1359-4184.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
AB The reported linkage between **bipolar disorder** and a large pericentric portion of **chromosome 18** has been replicated in an independent study. Further examination of this region showed that 18p11.2 had the greatest allele sharing in our pedigrees and increased sharing in other independently ascertained pedigree series permitting refinement of the region of significance. To facilitate positional cloning of a susceptibility gene, we used a combination of mapping reagents, including a subchromosomal somatic cell hybrid panel, a contig of clones in yeast artificial chromosomes (YAC), and a radiation hybrid (RH) panel, to construct a high resolution physical map of the region including sequence tag sites (STSs) and expressed sequence tags (ESTs). This approach generated the interlocus distance and order of 15 STSs and 16 ESTs including four novel transcripts, with an average of approximately 200 kb between loci, over a approximately

6-Mb region. This high resolution integrated map will be an important tool in providing loci for contig construction, and positional candidates for **mutation** screening.

L11 ANSWER 11 OF 24 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97348147 EMBASE
DN 1997348147
TI An integrated physical map of 18p11.2: A susceptibility region for **bipolar disorder**.
AU Esterling L.E.; Matise T.C.; Sanders A.R.; Yoshikawa T.; Overhauser J.; Gershon E.S.; Moskowitz M.T.; Detera-Wadleigh S.D.
CS L.E. Esterling, Clinical Neurogenetics Branch, National Institute of Mental Health, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892-1274, United States. lesterlg@pop.nidcd.nih.gov
SO Molecular Psychiatry, (1997) 2/5 (501-504).
Refs: 16
ISSN: 1359-4184 CODEN: MOPSFQ
CY United Kingdom
DT Journal; Article
FS 022 Human Genetics
032 Psychiatry
LA English
SL English
AB The reported linkage between **bipolar disorder** and a large pericentric portion of **chromosome 18** has been replicated in an independent study. Further examination of this region showed that 18p11.2 had the greatest allele sharing in our pedigrees and increased sharing in other independently ascertained pedigree series permitting refinement of the region of significance. To facilitate positional cloning of a susceptibility gene, we used a combination of mapping reagents, including a subchromosomal somatic cell hybrid panel, a contig of clones in yeast artificial chromosomes (YAC), and a radiation hybrid (RH) panel, to construct a high resolution physical map of the region including sequence tag sites (STSs) and expressed sequence tags (ESTs). This approach generated the interlocus distance and order of 15 STSs and 16 ESTs including four novel transcripts, with an average of .apprx. 200 kb between loci over a .apprx. 6-Mb region. This high resolution integrated map will be an important tool in providing loci for contig construction, and positional candidates for **mutation** screening.

L11 ANSWER 12 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:425337 SCISEARCH
GA The Genuine Article (R) Number: XA799
TI **Bipolar disorder**: From families to genes
AU Alda M (Reprint)
CS ROYAL OTTAWA HOSP, OTTAWA, ON K1Z 7K4, CANADA (Reprint); UNIV OTTAWA, DEPT PSYCHIAT, OTTAWA, ON K1N 6N5, CANADA

CYA CANADA
SO CANADIAN JOURNAL OF PSYCHIATRY-REVUE CANADIENNE DE PSYCHIATRIE, (MAY 1997) Vol. 42, No. 4, pp. 378-387.
Publisher: CANADIAN PSYCHIATRIC ASSOC, SUITE 200, 237 ARGYLE AVE, OTTAWA ON K2P 1B8, CANADA.
ISSN: 0706-7437.
DT General Review; Journal
FS CLIN; SOCSEARCH
LA English
REC Reference Count: 155
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Genetic factors are known to contribute to the etiology of bipolar illness, but the actual genetic mechanisms remain to be clarified.

Methods: This paper reviews the research undertaken to establish the generic basis of bipolar illness and to elucidate the nature of its genetic predisposition.

Results: The presented findings suggest that **bipolar affective disorder** is a heterogeneous condition characterized by a complex relationship between the genetic susceptibility and the clinical presentation. Linkage studies have generated promising and replicated findings on **chromosomes 18** and 21.

Conclusion: In spite of the methodological difficulties inherent in the generic study of psychiatric disorders, recent investigations have made important advances and promise to identify specific susceptibility genes.

L11 ANSWER 13 OF 24 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:111582 BIOSIS
DN PREV199800111582
TI **Bipolar affective disorder**: Genomic screen and follow-up analyses on chromosomes 4, 5, 7, 8, 12, 18, and 20.
AU McInnis, M. G. (1); Koskella, R. J.; McMahon, F. J.; Simpson, S. G. (1); Mackinnon, D. F. (1); Xu, J. (1); Meyers, D. A. (1); Friddle, C.; Breschel, T. S. (1); Botstein, D.; Depaulo, J. R. (1)
CS (1) Johns Hopkins Univ. Sch. Med., Baltimore, MD USA
SO American Journal of Human Genetics, (Oct., 1997) Vol. 61, No. 4 SUPPL., pp. A285.
Meeting Info.: 47th Annual Meeting of the American Society of Human Genetics Baltimore, Maryland, USA October 28-November 1, 1997
ISSN: 0002-9297.
DT Conference
LA English

L11 ANSWER 14 OF 24 MEDLINE DUPLICATE 7
AN 1998019047 MEDLINE
DN 98019047

TI Linkage analysis of manic depression (**bipolar affective disorder**) in Icelandic and British kindreds using markers on the short arm of **chromosome 18**.

AU Kalsi G; Smyth C; Brynjolfsson J; Sherrington R S; O'Neill J; Curtis D; Rifkin L; Murphy P; Petursson H; Gurling H M

CS Molecular Psychiatry Laboratory, University College London Medical School, UK.

SO HUMAN HEREDITY, (1997 Sep-Oct) 47 (5) 268-78.
Journal code: GE9. ISSN: 0001-5652.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199802

EW 19980204

AB Attempts were made to follow up results of a previous linkage study which suggested that a locus-modifying susceptibility to **bipolar** and related unipolar **affective disorder** might be present in the pericentromeric region of the short arm of **chromosome 18**. Twenty-three multiply affected pedigrees collected from Iceland and the UK were genotyped using three highly **polymorphic** microsatellite markers at D18S37, D18S40 and D18S44 which span the region implicated. Lod score analyses under the assumption of heterogeneity and non-parametric linkage analyses were performed. The total lod scores obtained were strongly negative, and analysis allowing for heterogeneity did not suggest that any subgroup of the families was linked. Model-free linkage analysis using extended relative pair analysis and MFLINK also failed to detect any evidence for linkage. Our study provides no support for the presence of a locus-modifying genetic susceptibility to **bipolar affective disorder** in the pericentromeric region of chromosome 18q11. Further analyses in independent samples should help to reveal whether our negative results are due to locus heterogeneity or whether the original results were false-positive.

L11 ANSWER 15 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)

AN 97:417124 SCISEARCH

GA The Genuine Article (R) Number: XA066

TI Molecular genetics of mental **disorders** with particular reference to **affective disorders**

AU Souery D; Lipp O; Mahieu B; Mendlewicz J (Reprint)

CS UNIV CLIN BRUSSELS, ERASME HOSP, DEPT PSYCHIAT, 808 ROUTE DE LENNIK, B-1070 BRUSSELS, BELGIUM (Reprint); UNIV CLIN BRUSSELS, ERASME HOSP, DEPT PSYCHIAT, B-1070 BRUSSELS, BELGIUM

CYA BELGIUM

SO EUROPEAN PSYCHIATRY, (MAY-JUN 1997) Vol. 12, Supp. [2], pp. S63-S69.
Publisher: EDITIONS SCIENTIFIQUES MEDICALES ELSEVIER, 141 RUE JAVEL,

75747 PARIS CEDEX 15, FRANCE.
ISSN: 0924-9338.
DT Article; Journal
FS CLIN
LA English
REC Reference Count: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The present article reviews the recent molecular genetic findings in **affective disorders**. Results of linkage and association studies are discussed in regard to the main limitations of these approaches in psychiatric **disorders**. On the whole, linkage and association studies contributed to the localisation of some potential vulnerability genes for **Bipolar affective disorder** on **chromosomes 18**, 5, 11, 4, 21 and X. The hypothesis of anticipation in **affective disorders** is also considered in light of interesting results with trinucleotide repeat **mutations**.

L11 ANSWER 16 OF 24 LIFESCI COPYRIGHT 1999 CSA
AN 96:103821 LIFESCI
TI Detection of linkage to **affective disorders** in the catalogued Amish pedigrees: A reply to Pauls et al.
AU Gershon, E.S.
CS Natl. Inst. Health, Bethesda, MD 20892-1274, USA
SO AM. J. HUM. GENET., (1996) vol. 58, no. 6, pp. 1381-1384.
ISSN: 0002-9297.
DT Journal
FS G
LA English
AB We have reported evidence for linkage of a region of **chromosome 18** markers to **affective** illness in 22 **bipolar** (**BP**) pedigrees. The pedigree series included 21 U.S. pedigrees collected by us and part of Amish pedigree 884 (NIGMS Human Genetic **Mutant** Cell Repository 1995) referred to as panel 3 in the catalog and also known as "the right extension." The rest of 884 was never genotyped by us, because it did not fit the criteria for inclusion, as described elsewhere. Pauls et al. have recently studied whether this linkage can be detected in the entire catalogued Amish pedigrees (884 and 1075) (NIGMS Human Genetic **Mutant** Cell Repository 1995) in four of the marker loci reported by Berrettini et al. The authors conclude that the Amish data contain no significant susceptibility locus for **BP** illness in this region of **chromosome 18**. We find that the data published by Pauls et al. are not conclusive with regard to the presence or absence of any susceptibility locus under the nonparametric analyses presented, and, although the sample size is extremely small, it could also be interpreted as consistent with our findings. In

Berrettini et al., evidence for linkage was found with affected-sib-pair (ASP) and multilocus affected-pedigree-member (APM) analyses. Affection status models were affection status model 1 (ASM1), which includes **BPI** and BP2 and schizoaffective (SA), and ASM2, which included ASM1 and recurrent unipolar **disorder** (UP); the quoted statistics that follow are from ASM2. Multilocus APM analysis showed significant sharing of marker alleles among affected persons, for five contiguous markers (D18S40, D18S45, D18S44, D18S66, and D18S56), with P values from <1 x 10 super(-4) to 7 x 10 super(-4) under weighting functions f(p) = 1 and f(p) = 1/ square root p. Since publication, we have performed multilocus ASP analysis. The P values for the multilocus analyses ranged between .003 and .00008, depending on the set of markers analyzed. LOD Score Analyses with Specified Genetic Model. Under a dominant model, Pauls et al. found a maximum LOD score of 1.31 for D18S53 in the right extension under an affection status model that includes **BP disorder** and major depression, which is about the same as that found for this pedigree by Berrettini et al. (LOD score = 1.25). When the rest of the pedigrees were included, the LOD score was >-2. Pauls et al. imply that the observed LOD scores in the right extension are a "false positive," finding them reminiscent of previous reports of linkage of this pedigree on chromosome 11p15 (which did not replicate). They assert that the "right extension" of Amish pedigree is more likely to have false-positive results than the other Amish pedigrees. In a simulation study they perform, where the marker was unlinked to the **disease** gene, 2.6% of the replicates gave a LOD score >1.0 for the right-extension pedigree but only 0.6% of replicates of the rest of the pedigrees had LOD scores >1.0. The argument that the false-positive rate in the first pedigree is too high is flawed, because, asymptotically, one would expect a LOD score of 1.0 to occur 3.2% of the time (assuming a two-tailed chi super(2) test). Thus the finding that 2.6% of replicates have this value is consistent with theory and does not suggest that this pedigree is prone to false-positive results. Their further assertion that "presumably, these observations also hold true for non-parametric (ASP) linkage analyses" is a speculation based on their incorrect interpretation. LOD scores of greater than or equal to 1 were reported by us in the 1994 paper only as illustrative results in single pedigrees, and not as a positive linkage result in any one pedigree or in the entire series.

L11 ANSWER 17 OF 24 MEDLINE DUPLICATE 8
AN 96301288 MEDLINE
DN 96301288
TI Analysis of **chromosome 18** DNA markers in multiplex pedigrees with manic depression.
AU Coon H; Hoff M; Holik J; Hadley D; Fang N; Reimherr F; Wender P; Byerley W

CS Department of Psychiatry, University of Utah Medical School, Salt Lake City 84121, USA.
NC MH-44212 (NIMH)
MH10168-F32 (NIMH)
MO1-RR00064 (NCRR)
+
SO BIOLOGICAL PSYCHIATRY, (1996 Apr 15) 39 (8) 689-96.
Journal code: A3S. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
AB Six pedigrees segregating manic-depressive illness (MDI) were analyzed for linkage to 21 highly **polymorphic** microsatellite DNA markers on **chromosome 18**. These markers span almost the entire length of the chromosome, and gaps between markers are less than 20 cM. In particular, we analyzed several markers localizing to the pericentromeric region of **chromosome 18** which generated lod scores suggestive of linkage in an independent study. Lod score analysis was performed and results were examined by family. One region produced positive lod scores, though at 18q23 and not in the pericentromeric region. We additionally used two nonparametric methods because the true mode of transmission of MDI is unknown; results were again somewhat suggestive for markers in the region of 18q23 but not in the pericentromeric region.

L11 ANSWER 18 OF 24 MEDLINE DUPLICATE 9
AN 96301287 MEDLINE
DN 96301287
TI Linkage analysis of families with bipolar illness and **chromosome 18** markers.
AU De bruyn A; Souery D; Mendelbaum K; Mendlewicz J; Van Broeckhoven C
CS Born Bunge Foundation, Department of Biochemistry, University of Antwerp (UIA), Belgium.
SO BIOLOGICAL PSYCHIATRY, (1996 Apr 15) 39 (8) 679-88.
Journal code: A3S. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
AB Linkage of **bipolar (BP)** illness with **chromosome 18** markers located at 18p11 was recently reported. A possible role for **chromosome 18** in the etiology of **BP** illness was implicated previously by the finding in three unrelated patients of a ring chromosome with breakpoints and deleted segments at 18pter-p11 and

18q23-qter. To test the potential importance of a gene defect on **chromosome 18** in our material, we examined linkage with **chromosome 18** markers in two families with multiple patients with **BP** illness or **BP** spectrum **disorders.** fourteen simple tandem repeat **polymorphisms** were used located in the chromosomal region 18p11 to 18q23 and separated by distances of approximately 10 cM on the genetic map. In one family linkage to **chromosome 18** could not be excluded. Linkage and segregation analysis in the family suggests that the 12-cM region between D18S51 and D18S61 located at 18q21.33-q23 may contain a candidate gene for **BP** illness.

L11 ANSWER 19 OF 24 MEDLINE
AN 97040879 MEDLINE
DN 97040879
TI Linkage disequilibrium analysis of G-olf alpha (GNAL) in **bipolar affective disorder.**
AU Tsiouris S J; Breschel T S; Xu J; McInnis M G; McMahon F J
CS Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1996 Sep 20) 67 (5) 491-4. Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
EW 19970304
AB This study examines G-olf alpha as a possible candidate gene for susceptibility to **bipolar affective disorder** (BPAD) using the Transmission Disequilibrium Test (TDT). G-olf alpha, which encodes a subunit of a G-protein involved in intracellular signaling, maps within a region of **chromosome 18** that has been implicated by two different linkage studies as a potential site of BPAD susceptibility loci. The expression pattern of G-olf alpha in the brain, its coupling to dopamine receptors, and the effects of lithium salts on G-proteins all support G-olf alpha as a candidate gene for BPAD. Our study population consisted of 106 probands and sibs with **bipolar** I **disorder**, with a median age-at-onset of 21.5 years ascertained from the United States. There was no evidence of linkage disequilibrium between BPAD and any of the observed G-olf alpha alleles in our sample. Division of families based on sex of the transmitting parent did not significantly change the results. This sample had good power (78%) to detect linkage disequilibrium with alleles conferring a relative risk equal to that estimated for the putative 18p locus (2.58). Our results do not support a major role for G-olf alpha as a susceptibility locus for BPAD in a

substantial portion of our sample. Other genes lying near G-olf alpha within the linked region on **chromosome 18** cannot be excluded by our data. This study illustrates the use of the TDT in evaluating candidate genes within linked chromosome regions.

L11 ANSWER 20 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:28440 SCISEARCH
GA The Genuine Article (R) Number: VZ757
TI A novel functional **polymorphism** within the promoter of the serotonin transporter gene: Possible role in susceptibility to **affective disorders**
AU Collier D A; Stober G; Li T; Heils A; Catalano M; DiBella D; Arranz M J; Murray R M; Vallada H P; Bengel D; Muller C R; Roberts G W; Smeraldi E; Kirov G; Sham P; Lesch K P (Reprint)
CS UNIV WURZBURG, DEPT PSYCHIAT, FUCHSLEINSTR 15, D-97080 WURZBURG, GERMANY (Reprint); UNIV WURZBURG, DEPT PSYCHIAT, D-97080 WURZBURG, GERMANY; DEPT PSYCHOL MED, MOL GENET SECT, LONDON SE5 8AF, ENGLAND; INST PSYCHIAT, DEPT NEUROPATHOL, LONDON SE5 8AF, ENGLAND; UNIV MILAN, OSPED SAN RAFFAELE, IRCCS, DEPT NEUROPSYCHIAT SCI, I-20127 MILAN, ITALY; UNIV WURZBURG, INST HUMAN GENET, D-97074 WURZBURG, GERMANY
CYA GERMANY; ENGLAND; ITALY
SO MOLECULAR PSYCHIATRY, (DEC 1996) Vol. 1, No. 6, pp. 453-460. Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE, HAMPSHIRE, ENGLAND RG21 6XS.
ISSN: 1359-4184.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The serotonin transporter (5-HTT) is a candidate locus for aetiological involvement in **affective disorders**. Biochemical studies in suicides and depressed patients suggest that 5-HT uptake function is frequently reduced in **affective** illness, Furthermore, 5-HTT is targeted by widely used antidepressant drugs such as fluoxetine, We have performed an association study of a short variant of the 5-HTT-linked **polymorphic** region (5-HTTLPR), which restricts transcriptional activity of the 5-HTT promoter leading to low functional expression of the 5-HTT, in 454 patients with **bipolar** or unipolar **affective disorder** and 570 controls, derived from three European Centres (London, Milan and Wurzburg). In all three centres, the frequency of the low activity allele was higher in patients than in controls (50% vs 45% in London, 45% vs 43% in Milan, 47% vs 40% in Wurzburg). Although these differences were not individually significant, a stratified analysis of all three samples gave a significant overall odds ratio

of 1.23 (95% confidence interval 1.02-1.49, P = 0.03). The excess of the homozygous low-activity genotype among the patients was even greater (odds ratio 1.53, 95% confidence interval 1.04-2.23, P = 0.02), suggesting partial recessivity of the low-activity allele, Given the functional role of 5-HTT, our findings suggest that 5-HTTLPR-dependent variation in functional 5-HTT expression is a potential genetic susceptibility factor for **affective disorders**, If this finding is replicated, further work on genetic variants with low 5-HTT activity may facilitate the differential diagnosis of affective **disorders**, the assessment of suicidal behaviour, and the prediction of good clinical response to antidepressants.

L11 ANSWER 21 OF 24 MEDLINE DUPLICATE 10
AN 96304711 MEDLINE
DN 96304711
TI Maternal inheritance and **chromosome 18** allele sharing in unilineal bipolar illness pedigrees.
AU Gershon E S; Badner J A; Detera-Wadleigh S D; Ferraro T N; Berrettini W H
CS National Institute of Mental Health, Bethesda, Maryland 20892-1274, USA.
NC 49181
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1996 Apr 9) 67 (2) 202-7. Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
AB We have replicated the observation of McMahon et al. [1995] that there is excess maternal transmission of illness in a series of previously described unilineal **Bipolar** manic-depressive illness extended pedigrees [Berrettini et al., 1991]. ("Transmission" is defined for any ill person in a pedigree when father or mother has a personal or immediate family history of major **affective disorder**.) We divided our pedigrees into exclusively maternal transmission (Mat) and mixed maternal-paternal transmission (in different pedigree branches) (Pat). Using affected sib-pair-analysis, linkage to a series of markers on chromosome 18p-cen was observed in the Pat but not the Mat pedigrees, with significantly greater identity by descent (IBD) at these markers in the Pat pedigrees. As compared with the pedigree series as a whole, the proportion of alleles IBD in the linkage region is much increased in the Pat pedigrees. As shown by Kruglyak and Lander [1995], as the sharing proportion of alleles in affected relative pairs increases, the number of such pairs needed to resolve the linkage region to a 1 cM interval becomes smaller. Genetic subdivision of an illness by clinical or pedigree configuration

criteria may thus play an important role in discovery of **disease** susceptibility **mutations**.

L11 ANSWER 22 OF 24 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 96:559755 SCISEARCH
GA The Genuine Article (R) Number: UY542
TI NO ASSOCIATION BETWEEN **CHROMOSOME-18** MARKERS AND LITHIUM-RESPONSIVE **AFFECTIVE-DISORDERS**
AU TURECKI G; ALDA M; GROF P; GROF E; MARTIN R; CAVAZZONI P A; DUFFY A; MACIEL P; ROULEAU G A (Reprint)
CS MONTREAL GEN HOSP, CTR RES NEUROSCI, 1650 CEDAR AVE, MONTREAL, PQ H3H 1A4, CANADA (Reprint); MONTREAL GEN HOSP, CTR RES NEUROSCI, MONTREAL, PQ H3H 1A4, CANADA; UNIV OTTAWA, ROYAL OTTAWA HOSP, AFFECT DISORDERS PROGRAM, OTTAWA, ON K1Z 7K4, CANADA
CYA CANADA
SO PSYCHIATRY RESEARCH, (26 JUN 1996) Vol. 63, No. 1, pp. 17-23. ISSN: 0165-1781.
DT Article; Journal
FS SOCSEARCH; LIFE
LA ENGLISH
REC Reference Count: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB An allelic association study of excellent responders to lithium was conducted with a candidate gene (G(olf),ln a G-protein receptor gene) and five other chromosome-18p markers. G(olf) is of special interest because it maps to a region of **chromosome 18** where two independent groups (Berrettini et al., 1994; Stine et al., 1995) have found linkage to **bipolar disorder**. It has been proposed that G proteins are involved in the pathogenesis of **bipolar disorder**, and lithium, an effective prophylactic agent, is known to impair G-protein activation. To reduce heterogeneity - a common obstacle to genetic investigation - only patients who showed excellent response to lithium prophylaxis were studied. Fifty-five genetically unrelated excellent responders to lithium prophylaxis were compared with 94 normal subjects of similar ethnic background. The groups did not differ in either allele or genotype frequency for the tested markers, The data do not support the hypothesis that the tested loci confer a major susceptibility for **affective disorders**.

L11 ANSWER 23 OF 24 MEDLINE DUPLICATE 11
AN 96065027 MEDLINE
DN 96065027
TI Evidence for linkage of **bipolar disorder** to **chromosome 18** with a parent-of-origin effect.
AU Stine O C; Xu J; Koskela R; McMahon F J; Gschwend M; Friddle C; Clark C D; McInnis M G; Simpson S G; Breschel T S; et al
CS Department of Psychiatry, Johns Hopkins University School of

Medicine, Baltimore, MD, USA.
SO AMERICAN JOURNAL OF HUMAN GENETICS, (1995 Dec) 57 (6) 1384-94.
Journal code: 3IM. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199604
AB A susceptibility gene on **chromosome 18** and a parent-of-origin effect have been suggested for **bipolar affective disorder** (BPAD). We have studied 28 nuclear families selected for apparent unilineal transmission of the BPAD phenotype, by using 31 **polymorphic** markers spanning **chromosome 18**. Evidence for linkage was tested with affected-sib-pair and LOD score methods under two definitions of the affected phenotype. The affected-sibpair analyses indicated excess allele sharing for markers on 18p within the region reported previously. The greatest sharing was at D18S37: 64% in **bipolar** and recurrent unipolar (RUP) sib pairs (P = .0006). In addition, excess sharing of the paternally, but not maternally, transmitted alleles was observed at three markers on 18q: at D18S41, 51 **bipolar** and RUP sib pairs were concordant for paternally transmitted alleles, and 21 pairs were discordant (P = 0004). The evidence for linkage to loci on both 18p and 18q was strongest in the 11 paternal pedigrees, i.e., those in which the father or one of the father's sibs is affected. In these pedigrees, the greatest allele sharing (81%; P = .00002) and the highest LOD score (3.51; phi = 0.0) were observed at D18S41. Our results provide further support for linkage of BPAD to **chromosome 18** and the first molecular evidence for a parent-of-origin effect operating in this **disorder**. The number of loci involved, and their precise location, require further study..

L11 ANSWER 24 OF 24 MEDLINE DUPLICATE 12
AN 96019068 MEDLINE
DN 96019068
TI Adrenocorticotropin receptor/melanocortin receptor-2 maps within a reported susceptibility region for bipolar illness on **chromosome 18**.
AU Detera-Wadleigh S D; Yoon S W; Berrettini W H; Goldin L R; Turner G; Yoshikawa T; Rollins D Y; Muniec D; Nurnberger J I Jr; Gershon E S
CS Clinical Neurogenetics Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland 20892, USA..
NC 1P41 RR03655 (NCRR)
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1995 Aug 14) 60 (4) 317-21.
Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199602
AB We have examined the possible linkage of adrenocorticotropin receptor/melanocortin receptor-2 (ACTHR/MC-2) to a reported putative susceptibility locus for **bipolar** illness (**BP**) in 20 affected pedigrees. Initially, allelic variants of the gene were identified by polymerase chain reaction-single stranded conformation **polymorphism** (PCR-SSCP) and the gene was genetically mapped using both the Centre d'Etudes du **Polymorphisme** Humain (CEPH) pedigrees and the **BP** pedigrees used in this study. We found that the ACTHR/MC-2 gene maps between D18S53 and D18S66. These loci span a region of **chromosome 18** which, in a previous study [Berrettini et al.: Proc Natl Acad Sci USA 91:5918-5921, 1994) revealed a putative predisposing locus to **BP** through nonparametric methods of linkage analysis. Linkage of ACTHR/MC-2 to **BP** was not demonstrable under parametric and nonparametric methods of analyses, although affected sib-pair (ASP) method revealed an increase in allele sharing among ill individuals, P = 0.023. Since this receptor is within a potential linkage region, ACTHR/MC-2 could be considered a candidate gene for **BP**.

=> d his l19- ful; d 1-15 .beverly

Named markers

(FILE 'CAPLUS' ENTERED AT 14:16:58 ON 05 MAR 1999)
L19 102 SEA ABB=ON PLU=ON (L1 OR L2 OR L5) AND MARKER
L20 21 SEA ABB=ON PLU=ON L19 AND (MUTAT? OR MUTAGEN? OR MUTANT OR POLYMORPH? OR POLY MORPH?)
L21 15 SEA ABB=ON PLU=ON L20 NOT (L4 OR L7)

L21 ANSWER 1 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1998:691590 CAPLUS
DN 130:93850
TI Serotonin transporter gene **polymorphisms** in patients with unipolar or bipolar depression
SO Neurosci. Lett. (1998), 255(3), 143-146
CODEN: NELED5; ISSN: 0304-3940
AU Bellivier, Frank; Henry, Chantal; Szoke, Andrei; Schurhoff, Franck; Nosten-Bertrand, Marika; Feingold, Josue; Launay, Jean-Marie; Leboyer, Marion; Laplanche, Jean-Louis
PY 1998
AB To explore the involvement of serotonin transporter (5HTT) in mood **disorder**, the authors studied 2 **polymorphisms** of the 5HTT gene (a variable no. of tandem repeats in the second intron (VNTR) and a 44 **bp** insertion/deletion in the 5HTT linked **polymorphic** region (5-HTTLPR)) in a sample of unipolar and **bipolar** patients and controls. Homozygosity for the short variant of the 5-HTTLPR was more frequent in bipolar patients than in controls, whereas there was no difference between bipolar

patients and controls for allele distribution, suggesting a recessive effect. The interaction between the 2 **markers** suggests that the 2 **polymorphisms** probably have independent effects to det. the susceptibility to **affective disorder**. Further studies are required to identify the precise phenotype assocd. with 5HTT **polymorphisms** in depressed patients.

L21 ANSWER 2 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1998:633914 CAPLUS
DN 130:50771
TI Self-esteem in remitted patients with mood disorders is not associated with the dopamine receptor D4 and the serotonin transporter genes
SO Psychiatry Res. (1998), 80(2), 137-144
CODEN: PSRSDR; ISSN: 0165-1781
AU Serretti, Alessandro; Macciardi, Fabio; Di Bella, Daniela; Catalano, Marco; Smeraldi, Enrico
PY 1998
AB Disturbances of the dopaminergic and serotoninergic neurotransmitter systems have been implicated in the pathogenesis of depressive symptoms. Assocns. have been reported between **markers** of the two neurotransmitter systems and the presence of illness or severity of depressive episodes, but no attention has been focused on the periods of remission. The present report focuses on a possible assocn. of self-esteem in remitted mood disorder patients with the functional **polymorphism** located in the upstream regulatory region of the serotonin transporter gene (5-HTTLPR) and the dopamine receptor D4 (DRD4). Inpatients (N = 162) affected by **bipolar** and unipolar **disorder** (DSM III-R) were assessed by the Self-Esteem Scale (SES, Rosenberg, 1965) and were typed for DRD4 and 5-HTTLPR (subjects) variants at the third exon using polymerase chain reaction (PCR) techniques. Neither DRD4 nor 5-HTTLPR variants were assocd. with SES scores, and consideration of possible stratification effects such as sex and psychiatric diagnosis did not reveal any assocn. either. The serotonin transporter and dopamine receptor D4 genes do not, therefore, influence self-esteem in remitted mood disorder subjects.

L21 ANSWER 3 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1998:633913 CAPLUS
DN 130:50770
TI Dopamine receptor D4 gene is associated with delusional symptomatology in mood disorders
SO Psychiatry Res. (1998), 80(2), 129-136
CODEN: PSRSDR; ISSN: 0165-1781
AU Serretti, Alessandro; Macciardi, Fabio; Cusin, Cristina; Lattuada, Enrico; Lilli, Roberta; Smeraldi, Enrico
PY 1998

AB Disturbances of the dopaminergic neurotransmitter system have been implicated in the pathogenesis of depressive symptoms. Many studies have, however, failed to detect any assocn. between genetic **markers** for the dopamine system and mood disorders. A possible reason for this may lie in the definition of phenotype, which is traditionally based on psychiatric diagnosis. In this study, the authors investigated the possibility that functional variants of the dopamine D4 receptor (DRD4) gene might be assocd. with depressive symptomatol. in a sample of mood disorder subjects. Seventy-nine inpatients affected by **bipolar** and major depressive **disorder** (DSM-IV) were assessed at admission by the Hamilton Depression Rating Scale and were typed for DRD4 variants at the third exon using polymerase chain reaction (PCR) techniques. DRD4 was assocd. with delusional symptoms, with DRD4*7 exhibiting higher scores when compared to DRD4* variants. Polarity of mood disorder did not influence the results significantly. The findings are in accordance with the authors' previous report of an assocn. of the DRD4 gene with delusional symptomatol. of major psychoses. DRD4*7 should, therefore, be considered a liability factor for delusional symptoms in mood disorders.

L21 ANSWER 4 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1998:613387 CAPLUS
TI Variability in the serotonin transporter gene and increased risk for major depression with melancholia
SO Hum. Genet. (1998), 103(3), 319-322
CODEN: HUGEDQ; ISSN: 0340-6717
AU Gutierrez, Blanca; Pintor, Luis; Gasto, Cristobal; Rosa, Araceli; Bertranpetit, Jaume; Vieta, Eduard; Fananas, L.
PY 1998
AB The serotonin transporter (SERT) gene is a particularly interesting candidate for genetic involvement in **affective disorders** owing to its role in both the regulation of serotonergic neurotransmission and the mechanism of action of many antidepressant drugs. In this study, variability in the SERT gene was analyzed for the first time in a sample of patients with major depression with melancholia (MDDM) in the context of a genetic assocn. study. Two different **polymorphisms** of the SERT gene (17q11.1-17q12) were analyzed: a variable no. of tandem repeats (VNTR) **polymorphism** in intron 2, and a deletion/insertion **polymorphism** (5-HTTLPR) in the promoter region of the gene, the short variant of which (allele 484) reduces the transcriptional efficiency of the SERT gene. Our sample consisted of 74 unrelated subjects who strictly met DSM-IV criteria for MDDM and 84 healthy controls, all of Spanish origin. The anal. of haplotype distribution for both **polymorphisms** showed significant differences between cases and controls (log-likelihood ratio .chi.2=11.15, df=4, P=0.025). Moreover, when the frequencies of the 484-STin2.10 haplotype were considered in comparison with any other

haplotype combination, a significant increase in this haplotype was found in patients with MDDM [z=2.53 (95% CI, 1.21-5.34), P=0.007]. According to these results, variability in the SERT gene has a small effect on liability to MDDM. Our findings are compatible with an additive effect of both the 484 low-activity allele and a **mutation** elsewhere within the transporter gene or a susceptibility locus nearby in linkage disequil. with the VNTR **marker**.

L21 ANSWER 5 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1998:574163 CAPLUS
DN 129:340335
TI A susceptibility locus for **bipolar affective disorder** on chromosome 4q35
SO Am. J. Hum. Genet. (1998), 62(5), 1084-1091
CODEN: AJHGAG; ISSN: 0002-9297
AU Adams, Linda J.; Mitchell, Philip B.; Fielder, Sharon L.; Rosso, Amanda; Donald, Jennifer A.; Schofield, Peter R.
PY 1998
AB **Bipolar affective disorder** (**BAD**) affects .apprx.1% of the population and shows strong heritability. To identify potential BAD susceptibility loci, the authors undertook a 15-cM genome screen, using 214 microsatellite **markers** on the 35 most informative individuals of a large, statistically powerful pedigree. Data were analyzed by parametric two-point linkage methods under several diagnostic models. LOD scores >1.00 were obtained for 21 **markers**, with four of these >2.00 for at least one model. The remaining 52 individuals in the family were genotyped with these four **markers**, and LOD scores remained pos. for three **markers**. A more intensive screen was undertaken in these regions, with the most pos. results being obtained for chromosome 4q35. Using a dominant model of inheritance with 90% max. age-specific penetrance and including bipolar I, II, schizoaffective/mania, and unipolar individuals as affected, the authors obtained a max. two-point LOD score of 2.20 (.theta. =.15) at D4S1652 and a max. three-point LOD score of 3.19 between D4S408 and D4S2924. Nonparametric analyses further supported the presence of a locus on chromosome 4q35. A max. score of 2.62 was obtained between D4S1652 and D4S171 by use of the GENEHUNTER program, and a max. score of 3.57 was obtained at D4S2924 using the affected pedigree member method. Anal. of a further 10 pedigrees suggests the presence of this locus in at least one addnl. family, indicating a possible predisposing locus and not a pedigree-specific **mutation**. The authors' results suggest the presence of a novel BAD susceptibility locus on chromosome 4q35.

L21 ANSWER 6 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1997:299689 CAPLUS
DN 126:273271

TI Human serotonin transporter gene allele VNTR region sequences and use in screening and diagnosis of disorders of serotonergic dysfunction

SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2

IN Battersby, Sharon; Fink, George; Goodwin, Guy Manning; Harmar, Anthony John; Ogilvie, Alan David; Smith, Christopher Albert Dale

APPLICATION NO.	DATE
WO 96-GB2360	19960923
AU 96-70898	19960923
GB 98-5376	19960923

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9711175	A1	19970327	WO 96-GB2360	19960923
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
AU 9670898	A1	19970409	AU 96-70898	19960923
GB 2321246	A1	19980722	GB 98-5376	19960923

PY 1997
1997
1998

AB Three novel alleles of the serotonin transporter gene are disclosed and shown to be effective **markers** for screening and diagnosis of migraine and psychiatric disorders. The sequences of the alleles are given. Methods for in vitro screening of individuals using DNA taken from blood samples are included. Patients with unipolar or **bipolar affective disorder** or with common or classical migraine (migraine without aura or migraine with aura, resp.) were tested for the various alleles, STin2.12, Stin2.9, or Stin2.10. PCR, SSCP, LCR and Southern blot methods are included.

L21 ANSWER 7 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1997:128253 CAPLUS
DN 126:207986
TI Two-locus admixture linkage analysis of **bipolar** and unipolar **affective disorder** supports the presence of susceptibility loci on chromosomes 11p15 and 21q22
SO Genomics (1997), 39(3), 271-278
CODEN: GNMCEP; ISSN: 0888-7543
AU Smyth, Ciaran; Kalsi, Gursharan; Curtis, David; Brynjolfsson, Jon; O'Neill, Jane; Rifkin, Larry; Moloney, Eamon; Murphy, Patrice; Petursson, Hannes; Gurling, Hugh

PY 1997
AB Following a report of a linkage study that yielded evidence for a susceptibility locus for **bipolar affective disorder** on the long arm of chromosome 21, the authors studied 23 multiply affected pedigrees collected from Iceland and the UK, using the **markers** PFKL, D21S171, and D21S49. Counting only bipolar cases as affected, a two-point LOD of 1.28 was obtained using D21S171 (.theta. = 0.01, .alpha. = 0.35), with three Icelandic families producing LODs of 0.63, 0.62, and 1.74 (all at .theta. = 0.0). Affected sib pair anal. demonstrated increased allele sharing at D21S171 when unipolar cases were also considered affected. The same set of pedigrees had previously been typed for a tyrosine hydroxylase gene (TH) **polymorphism** at 11p15 and had shown some moderate evidence for linkage. When information from TH and the 21q **markers** was combined in a two-locus admixt. anal., an overall admixt. LOD of 3.87 was obtained using the bipolar affection model. Thus the data are compatible with the hypothesis that a locus at or near TH influences susceptibility in some pedigrees, while a locus near D21S171 is active in others. Similar analyses in other datasets should be carried out to confirm or refute the authors' tentative finding.

L21 ANSWER 8 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1997:38167 CAPLUS
DN 126:73334
TI Scanning the genome with 1772 microsatellite **markers** in search of a **bipolar disorder** susceptibility gene
SO Mol. Psychiatry (1996), 1(5), 404-407
CODEN: MOPSFQ; ISSN: 1359-4184
AU Polymeropoulos, M. H.; Schaffer, A. A.
PY 1996
AB **Bipolar disorder** affects approx. 1% of the population and there is evidence that genetic factors play an important role in the prodn. of symptoms. We undertook a genetic linkage study for the discovery of a major locus conferring susceptibility for bipolar illness in an Old Order Amish pedigree. Our study took advantage of publicly available phenotypic and genotypic information, the latter as a byproduct of the human genome project effort. We present a genomic scan using 1772 **polymorphic** genetic **markers** and we suggest candidate genetic regions for harboring a **bipolar disorder** susceptibility gene.

L21 ANSWER 9 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1995:190536 CAPLUS
DN 122:98359
TI A linkage study of **affective disorder** with DNA **markers** for the ABO-AK1-ORM linkage group near the dopamine beta hydroxylase gene

SO Biol. Psychiatry (1994), 36(7), 434-42
CODEN: BIPCBF; ISSN: 0006-3223
AU Sherrington, Robin; Curtis, David; Brynjolfsson, Jon; Moloney, Eamonn; Rifkin, Larry; Petursson, Hannes; Gurling, Hugh
PY 1994
AB Combining data from a no. of studies has provided evidence for a susceptibility allele for **affective disorder** near to the ABO-AK1-ORM region on chromosome 9q34. The dopamine beta hydroxylase gene locus is also at 9q34. Five multigenerational families with **bipolar** and unipolar **affective disorder** were analyzed for linkage with highly **polymorphic** microsatellite **markers** from the candidate region. The segregation of the illness in these families was compatible with an autosomal dominant susceptibility allele. Linkage analyses using conservative parameters seemed to provide strong evidence against a major susceptibility allele in this region including the candidate gene dopamine beta hydroxylase in these families.

L21 ANSWER 10 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1994:209709 CAPLUS
DN 120:209709
TI A genome-wide search for genes predisposing to manic-depression, assuming autosomal dominant inheritance
SO Am. J. Hum. Genet. (1993), 52(6), 1234-49
CODEN: AJHGAG; ISSN: 0002-9297
AU Coon, Hilary; Jensen, Steve; Hoff, Mark; Holik, John; Plaetke, Rosemarie; Reimherr, Fred; Wender, Paul; Leppert, Mark; Byerley, William
PY 1993
AB Manic-depressive illness (MDI), also known as "**bipolar affective disorder**," is a common and devastating neuropsychiatric illness. Although pivotal biochem. alterations underlying the disease are unknown, results of family, twin, and adoption studies consistently implicate genetic transmission in the pathogenesis of MDI. In order to carry out linkage anal., the authors ascertained eight moderately sized pedigrees contg. multiple cases of the disease. For a four-allele **marker** mapping 5 cM from the disease gene, the pedigree sample has >97% power to detect a dominant allele under genetic homogeneity and has >73% power under 20% heterogeneity. To date, the eight pedigrees have been genotyped with 328 **polymorphic** DNA loci throughout the genome. When autosomal dominant inheritance was assumed, 273 DNA **markers** gave lod scores <-2.0 at recombination fraction (.theta.) = .0, 174 DNA loci produced lod scores <-2.0 at .theta. = .05, and 4 DNA **marker** loci yielded lod scores >1 (chromosome 5-D5S39, D5S43, and D5S62; chromosome 11-D11S85). Of the **markers** giving lod scores >1, only D5S62 continued to show evidence for linkage when the affected-pedigree-member method

was used. The D5S62 locus maps to distal 5q, a region contg. neurotransmitter-receptor genes for dopamine, norepinephrine, glutamate, and gamma-aminobutyric acid. Although addnl. work in this region may be warranted, the authors' linkage results should be interpreted as preliminary data, as 68 unaffected individuals are not past the age of risk.

L21 ANSWER 11 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1993:618870 CAPLUS
DN 119:218870
TI Novel triplet repeat containing genes in human brain: Cloning, expression, and length **polymorphisms**
SO Genomics (1993), 16(3), 572-9
CODEN: GNMCEP; ISSN: 0888-7543
AU Li, Shi Hua; McInnis, Melvin G.; Margolis, Russell L.; Antonarakis, Stylianos E.; Ross, Christopher A.
PY 1993
AB Human genes contg. triplet repeats may markedly expand in length and cause neuropsychiatric disease, explaining the phenomenon of anticipation (increasing severity or earlier age of onset in successive generations in a pedigree). To identify novel genes with triplet repeats, the authors screened a human brain cDNA library with oligonucleotide probes contg. CTG or CCG triplet repeats. Fourteen of 40 clones encoded novel human genes, and 8 of these inserts have been sequenced on both strands. All contain repeats, and 5 of the 8 have 9 or more consecutive perfect repeats. All are expressed in brain. Chromosomal assignments reveal a distribution of these genes on multiple autosomes and the X-chromosome. Further, the repeat length in two of the genes is highly **polymorphic** , making them valuable index linkage **markers**. The authors predict that many triplet repeat-contg. genes exit; screening with the CTG probe suggests approx. 50-100 genes contg. this type of repeat are expressed in the human brain. Since addnl. **disorders** such as Huntington's **disease**, **bipolar affective disorder**, and possibly others, show features of anticipation, the authors suggest that these novel human genes with triplet repeats are candidates for causing neuropsychiatric **diseases**.

L21 ANSWER 12 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1990:17172 CAPLUS
DN 112:17172
TI Assignment of the gene for complete X-linked congenital stationary night blindess (CSNB1) to Xp11.3
SO Genomics (1989), 5(4), 727-37
CODEN: GNMCEP; ISSN: 0888-7543
AU Musarella, M. A.; Weleber, R. G.; Murphey, W. H.; Young, R. S. L.; Anson-Cartwright, L.; Mets, M.; Kraft, S. P.; Polemeno, R.; Litt, M.; Worton, R. G.

PY 1989
AB X-linked congenital stationary night blindness (CSNB) is a nonprogressive retinal **disorder** characterized by a presumptive defect of neurotransmission between the photoreceptor and **bipolar** cells. Carriers are not clin. detectable. A new classification for CSNB includes a complete type, which lacks rod function by electroretinog. and dark adaptometry, and an incomplete type, which shows some rod function on scotopic testing. The refraction in the complete CSNB patients ranges from mild to severe myopia; the incomplete ranges from moderate hyperopia to moderate myopia. To map the gene responsible for this disease, 8 multigeneration families were studied, 7 with complete (CSNB) (CSNB1) and 1 with incomplete CSNB, by linkage anal. using 17 **polymorphic** X-chromosome **markers**. Tight genetic linkage was found between CSNB1 and an Xp11.3 DNA **polymorphic** site, DXS7, in 7 families with CSNB1. No recombinations to CSNB1 were found with **marker** loci DXS7 and DXS14. The result with DXS14 may be due to the small no. of scored meioses (10). No linkage could be shown with Xq loci PGK, DXYS1, DXS52, and DXS15. Pairwise linkage anal. maps the gene for CSNB1 at Xp 11.3 and suggests that the CSNB1 locus is distal to another Xp11 **marker**, TIMP, and proximal to the OTC locus. Five-point anal. on the 8 families supported the order DXS7-CSNB1-TIMP-DXS255-DXS14. The odds in favor of this order were 9863:1. Removal of the family with incomplete CSNB (F21) revealed 2 most favored orders, DXS7-CSNB1-TIMP-DXS255-DXS14 and CSNB1-DXS7-TIMP-DXS255-DXS14. Heterogeneity testing using the CSNB1-M27.beta. and CSNB1-TIMP linkage data (DXS7 was not informative in F21) was not significant to support evidence of genetic heterogeneity.

L21 ANSWER 13 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1987:132942 CAPLUS
DN 106:132942
TI **Bipolar affective disorders** linked to DNA **markers** on chromosome 11
SO Nature (London) (1987), 325(6107), 783-7
CODEN: NATUAS; ISSN: 0028-0836
AU Egeland, Janice A.; Gerhard, Daniela S.; Pauls, David L.; Sussex, James N.; Kidd, Kenneth K.; Allen, Cleona R.; Hostetter, Abram M.; Housman, David E.
PY 1987
AB An anal. of the segregation of restriction fragment length **polymorphisms** in an Old Order Amish pedigree has made it possible to localize a dominant gene conferring a strong predisposition to manic depressive disease to the tip of the short arm of chromosome 11.

L21 ANSWER 14 OF 15 CAPLUS COPYRIGHT 1999 ACS

AN 1987:99990 CAPLUS
DN 106:99990
TI Linkage of tyrosine hydroxylase to four other **markers** on the short arm of chromosome 11
SO Nucleic Acids Res. (1986), 14(24), 9927-32
CODEN: NARHAD; ISSN: 0305-1048
AU Moss, P. A. H.; Davies, K. E.; Boni, C.; Mallet, J.; Reeders, S. T.
PY 1986
AB Tyrosine hydroxylase is the rate-limiting enzyme in catecholamine synthesis; the gene has previously been cloned and localized to the short arm of chromosome 11. Because of the interest in tyrosine hydroxylase as a candidate gene for manic-depressive psychosis and other **affective disorders**, family studies were performed to det. the linkage of tyrosine hydroxylase with insulin, .beta.-globin, D11S12, and Harvey-ras 1, members of a linkage group which has previously been localized to 11p. Anal. of DNA from the Center d'Etude du **Polymorphisme** Humain (CEPH) and from 2 large British pedigrees showed that tyrosine hydroxylase is closely linked to these 4 loci (.cxa. = 7.36, .theta. = 0.04 for linkage to insulin) and suggest a gene order based on multipoint mapping.

L21 ANSWER 15 OF 15 CAPLUS COPYRIGHT 1999 ACS
AN 1982:179077 CAPLUS
DN 96:179077
TI Segregation and linkage studies of plasma dopamine-.beta.-hydroxylase (DBH), erythrocyte catechol-O-methyltransferase (COMT), and platelet monoamine oxidase (MAO): possible linkage between the ABO locus and a gene controlling DBH activity
SO Am. J. Hum. Genet. (1982), 34(2), 250-62
CODEN: AJHGAG; ISSN: 0002-9297
AU Goldin, Lynn R.; Gershon, Elliot S.; Lake, C. Raymond; Murphy, Dennis L.; McGinniss, Mary; Sparkes, Robert S.
PY 1982
AB Measurements of DBH, COMT, and MAO along with 27 **polymorphic marker** phenotypes were available for 162 patients with major **affective disorders** and 1,125 of their relatives. Levels of enzymes were previously found not to be assocd. with illness. Pedigree anal. methods for quant. traits are used to test single-gene hypotheses for segregation of DBH in 32 families with 411 individuals, COMT in 30 families with 351 individuals, and MAO in 50 families with 309 individuals. The familial distribution of both DBH and COMT are consistent with 2 codominant alleles at the same locus that account for 56% and 59% of the total variance, resp.,. MAO activity cannot be shown to be segregating as a single major gene, but a purely nongenetic hypothesis is also rejected. A possible linkage of a locus for DBH to the ABO locus is indicated by a max. lod score of 1.82 at 0% and 10% recombination fractions for males and females, resp. A lod score of 0.61 at 0% recombination for a similar anal. in a single large pedigree was reported by R. C.

Elston et al. (1979) making the combined lod score for the 2 studies equal to 2.32 at 0% recombination.

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=> d his 122- ful

     (FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI,
     SCISEARCH, JICST-EPLUS, PROMT' ENTERED AT 14:22:57 ON 05 MAR 1999)
L22          407 SEA ABB=ON  PLU=ON  L20
L23            0 SEA ABB=ON  PLU=ON  L22 AND (SAVA5 OR GA203 OR D18S1140
                 OR D18(W)("S1140" OR "S59") OR W3422 OR AT201 OR D18S59)

=> d his l24- ful; d 1-6 .beverly

     (FILE 'CAPLUS' ENTERED AT 14:30:09 ON 05 MAR 1999)
L24            6 SEA ABB=ON  PLU=ON  SAVA5 OR GA203 OR D18S1140 OR
                 D18(W)("S1140" OR "S59") OR W3422 OR AT201 OR D18S59
L25            6 SEA ABB=ON  PLU=ON  L24 NOT (L4 OR L7)

L25  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 1999 ACS
AN   1999:95928  CAPLUS
TI   Novel regions of allelic deletion on chromosome 18p in tumors of the
     lung, brain and breast
SO   Oncogene (1998), 17(26), 3499-3505
     CODEN: ONCNES; ISSN: 0950-9232
AU   Tran, Yen; Benbatoul, Khalid; Gorse, Karen; Rempel, Sandra; Futreal,
     Andrew; Green, Mark; Newsham, Irene
PY   1998
AB   Lung cancer is now the no. one cause of cancer death for both men
     and women.  An age-adjusted anal. over the past 25 yr shows that in
     women specifically, lung cancer incidence is on the rise.  It is
     estd. that 10-20 genetic events including the alteration of
     oncogenes and tumor suppressor genes will have occurred by the time
     a lung tumor becomes clin. evident.  In an effort to identify
     regions contg. novel cancer genes, chromosome 18p11, a band not
     previously implicated in disease, was examd. for loss of
     heterozygosity (LOH).  In this study, 50 matched normal and NSCLC
     tumor samples were examd. using six 18p11 and one 18q12.3 PCR-based
     polymorphic markers.  In addn., LOH was examd. in 29 glioblastoma
     pairs and 14 paired breast carcinomas.  This anal. has revealed
     potentially two regions of LOH in 18p11 in up to 38% of the tumor
     samples examd.  The regions of LOH identified included a 2 cm area
     between markers D18S59 and D18S476, and a more proximal,
     25 cm region of intermediate frequency between D18S452 and D18S453.
     These results provide evidence for the presence of one or more
     potential tumor suppressor genes on the short arm of chromosome 18
     which may be involved in NSCLC, brain tumors and possibly breast
     carcinomas as well.

L25  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 1999 ACS
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AN 1998:792792 CAPLUS
TI Evidence that a locus for familial high myopia maps to chromosome 18p
SO Am. J. Hum. Genet. (1998), 63(1), 109-119
CODEN: AJHGAG; ISSN: 0002-9297
AU Young, Terri L.; Ronan, Shawn M.; Drahozal, Leslie A.; Wildenberg, Scott C.; Alvear, Alison B.; Oetting, William S.; Atwood, Larry D.; Wilkin, Douglas J.; King, Richard A.
PY 1998
AB Myopia, or nearsightedness, is the most common human eye disorder. A genomewide screen was conducted to map the gene(s) assocd. with high, early-onset, autosomal dominant myopia. Eight families that each included two or more individuals with .gtoreq. -6.00 diopters (D) myopia, in two or more successive generations, were identified. Myopic individuals had no clin. evidence of connective-tissue abnormalities, and the av. age at diagnosis of myopia was 6.8 yr. The av. spherical component refractive error for the affected individuals was -9.48 D. The families contained 82 individuals; of these, DNA was available for 71 (37 affected). Markers flanking or intragenic to the genes for Stickler syndrome types 1 and 2 (chromosomes 12q13.1-q13.3 and 6p21.3, resp.), Marfan syndrome (chromosome 15q21.1), and juvenile glaucoma (chromosome 1q21-q31) were also analyzed. No evidence of linkage was found for markers for the Stickler syndrome types 1 and 2, the Marfan syndrome, or the juvenile glaucoma loci. After a genomewide search, evidence of significant linkage was found on chromosome 18p. The max. LOD score was 9.59, with marker D18S481, at a recombination fraction of .0010. Haplotype anal. further refined this myopia locus to a 7.6-cM interval between markers **D18S59** and D18S1138 on 18p11.31.

L25 ANSWER 3 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1991:447369 CAPLUS
DN 115:47369
TI Molecular cloning and expression of Mycobacterium tuberculosis Aoyama B peptide antigen genes in Escherichia coli. A gene encoding a 60kD antigen (**AT201**) and the immunological activity of recombinant peptides (15 and 60kD)
SO Kekkaku (1990), 65(8), 507-17
CODEN: KEKKAG; ISSN: 0022-9776
AU Tanaka-Hayashi, Tomoko; Tsuyuguchi, Takaichi; Aoyama, Kazue; Okamura, Haruki; Nagata, Kumiko; Tamura, Toshihide; Yamamoto, Yoshihiro; Furuyama, Junichi; Komatsu, Toshinori; Shin-ka, Sohei
PY 1990
AB To obtain recombinant peptides related to PPDs, a genomic library was constructed from the DNA of M. tuberculosis Aoyama B, a std. strain in Japan to manuf. PPDs, using the plasmid vector pUC18 series. Seven clones reacting with anti-PPD rabbit serum on immunoblotting were obtained, and the restriction map was analyzed. In this study, the nucleotide sequence of a 60 kD peptide gene was

detd., and the comparative database anal. (GENBANK) revealed a striking level of homol. to mycobacterial heat shock protein. The expression mode of pAT201 encoding the 60 kD, as well as pAT01 encoding the 15 kD peptide, indicated that these peptides were not hybrid proteins with the lacZ gene product, but that they consisted of mycobacterial peptides only. Therefore, 15 kD and 60 kD were subjected directly to immunol. studies. The peptides were extd. from E. coli, carrying pAT01 or pAT201, purified by DEAE chromatog. and followed by Detoxi-Gel to remove LPS. The 15 kD peptide behaved similarly to PPDs both in the DTH skin reaction and the lymphocyte proliferation response on guinea pigs or rats with respect to sensitivity. However, 60 kD was unique in that it behaved like a general mitogen. The role of the 60 kD peptide was compared to the common antigen, generaly found in most species of bacteria as the heat shock protein.

L25 ANSWER 4 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1987:584621 CAPLUS
DN 107:184621
TI Study of interaction and some properties in a sodium oxide-zinc oxide-gallium(III) oxide-water system
SO Zh. Prikl. Khim. (Leningrad) (1987), 60(8), 1696-701
CODEN: ZPKHAB; ISSN: 0044-4618
AU Khayak, V. G.; Yatsenko, S. P.; Diev, V. N.
PY 1987
AB Addn. of **Ga203** to alk. zincate solns. lowers ZnO soly. significantly, esp. in the region where the liq. phase is in equil. with both Na2O.3.8ZnO.6H2O and Na2O.2.4ZnO.5.4H2O. The ZnO soly. decreases as Na2O concn. decreases from 20-25 to 8-10 wt.%. Favorable conditions for concg. Ga for subsequent sepn. require a Na2O content .ltoreq.10-12 wt.%. Soln. densities and viscosities increase as Na2O concn. increases, while sp. elec. cond. decreases as Na2O and Ga2O3 concns. decrease.

L25 ANSWER 5 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1978:451747 CAPLUS
DN 89:51747
TI Precipitation in nonstoichiometric magnesium gallium oxide (Mg1-3xGa2+2x.box.xO4) spinels
SO J. Phys. (Paris), Colloq. (1977), (7), 80-3
CODEN: JPQCAK
AU Bassoul, P.; Lefebvre, A.; Gilles, J. C.
PY 1977
AB The formation of an intermediate metastable phase before the final MgGa2O4 + .beta.-G2O3 phase in nonstoichiometric MgGa2O4-**Ga203** spinels was studied. This phase has a 1-dimensional periodic antiphase domain structure derived from the spinel structure. The structures of both ppts. (.epsilon.Mg and .beta.-Ga2O3) are characterized by a monoclinic distortion of their

O framework. An invariant plane lattice strain describes the .gamma..fwdarw..epsilon.Mg transformation; this invariant plane is near the antiphase boundary plane and the habit plane which was obsd. in electronic microscopy. An invariant line lattice strain describes the .gamma.-.beta.-Ga2O3 transformation; this strain is not much different from a simple shear.

L25 ANSWER 6 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1972:493891 CAPLUS
DN 77:93891
TI Cross sections of the ternary system sodium oxide-boric oxide-gallium(III) oxide
SO Issled. Obl. Neorg. Fiz. Khim. (1971) 127-9
From: Ref. Zh., Khim. 1971, Abstr. No. 22B773
AU Rza-Zade, P. F.; Ganf. K. L.; Guseinova, S. A.
PY 1971
AB Some cross sections of Na2O.xB2O3-Ga2O3 (x = 1, 2, 3, 4) were studied by DTA and radiog., and the d. and microhardness of crystals and glasses were measured. The existence of congruently melting compds. was established: 2Na2O.**Ga2O3**.-2B2O3; Na2O.Ga2O3.B2O3, 2Na2O9Ga2O3.5B2O3. With x = 3 and 4, glasses contg. >65 mole % Ga2O3 were formed; their resistivity at room temp. was .apprx.1010 ohm-cm, their microhardness .apprx.456 kg/mm2, and their d.2.2-3.8 g/cm3.

=> d his l26- ful; d 1-5 bib abs

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT' ENTERED AT 14:31:23 ON 05 MAR 1999)
L26 66 SEA ABB=ON PLU=ON L24
L27 66 SEA ABB=ON PLU=ON L26 NOT L10
L28 7 SEA ABB=ON PLU=ON L27 AND (MUTAT? OR MUTAGEN? OR MUTANT OR POLYMORPH? OR POLY MORPH?)
L29 5 DUP REM L28 (2 DUPLICATES REMOVED)

L29 ANSWER 1 OF 5 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 1
AN 1999:109359 BIOSIS
DN PREV199900109359
TI Novel regions of allelic deletion on chromosome 18p in tumors of the lung, brain and breast.
AU Tran, Yen; Benbatoul, Khalid; Gorse, Karen; Rempel, Sandra; Futreal, Andrew; Green, Mark; Newsham, Irene (1)
CS (1) Theodore Gildred Cancer Cent., Dep. Med., Univ. Calif.-San Diego, La Jolla, CA 92093 USA
SO Oncogene, (Dec. 31, 1998) Vol. 17, No. 26, pp. 3499-3505.
ISSN: 0950-9232.
DT Article
LA English
AB Lung cancer is now the number one cause of cancer death for both men

and women. An age-adjusted analysis over the past 25 years shows that in women specifically, lung cancer incidence is on the rise. It is estimated that 10-20 genetic events including the alteration of oncogenes and tumor suppressor genes will have occurred by the time a lung tumor becomes clinically evident. In an effort to identify regions containing novel cancer genes, chromosome 18p11, a band not previously implicated in disease, was examined for loss of heterozygosity (LOH). In this study, 50 matched normal and NSCLC tumor samples were examined using six 18p11 and one 18q12.3 PCR-based **polymorphic** markers. In addition, LOH was examined in 29 glioblastoma pairs and 14 paired breast carcinomas. This analysis has revealed potentially two regions of LOH in 18p11 in up to 38% of the tumor samples examined. The regions of LOH identified included a 2 cm area between markers **D18S59** and D18S476, and a more proximal, 25 cm region of intermediate frequency between D18S452 and D18S453. These results provide evidence for the presence of one or more potential tumor suppressor genes on the short arm of chromosome 18 which may be involved in NSCLC, brain tumors and possibly breast carcinomas as well.

L29 ANSWER 2 OF 5 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:413683 SCISEARCH
GA The Genuine Article (R) Number: ZP648
TI No evidence of replication error phenotype in primary gastric lymphoma of mucosa-associated lymphoid tissue
AU Xu W S; Chan A C L; Liang R; Srivastava G (Reprint)
CS UNIV HONG KONG, DEPT PATHOL, UNIV PATHOL BLDG, QUEEN MARY HOSP COMPOUND, POKFUL, HONG KONG, PEOPLES R CHINA (Reprint); UNIV HONG KONG, DEPT PATHOL, HONG KONG, PEOPLES R CHINA; UNIV HONG KONG, DEPT MED, HONG KONG, PEOPLES R CHINA
CYA PEOPLES R CHINA
SO INTERNATIONAL JOURNAL OF CANCER, (29 MAY 1998) Vol. 76, No. 5, pp. 635-638.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0020-7136.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Replication error (RER) phenotype, caused by deficiency of DNA mismatch repair genes and revealed by widespread microsatellite instability, has been detected in subsets of a wide variety of solid tumors, but rarely in lymphomas in general. So far, the involvement of RER phenotype in the pathogenesis of gastric lymphoma of mucosa-associated lymphoid tissue (MALT) type has not been conclusively established. We therefore examined 9 microsatellite loci on 5 chromosomes [D2S123, D3S11, D3S1261, D3S1262, D3S1265,

D6S262, **D18S59**, a CTTT(T) repeat in intron 20 of RBI gene and a CA repeat in p53 locus] in 33 cases of primary gastric MALT lymphoma for evidence of microsatellite instability by polymerase chain reaction using primers end-labeled with [gamma-P-33] ATP. Although novel-length allele was observed in 7 of 33 cases (21.2%), none of these 7 cases showed changes in more than one locus. RER phenotype was scored as positive in a case when more than I of the 9 examined microsatellite loci showed length alterations. Accordingly, none of the 33 cases had a RER phenotype. This result suggests that the pathogenesis of gastric MALT lymphoma does not involve RER phenotype. It is consistent with the general observations in lymphomas, but is highly in contrast to a previous report showing more than 50% of MALT lymphomas with the RER phenotype. (C) 1998 Wiley-Liss, Inc.

L29 ANSWER 3 OF 5 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:904432 SCISEARCH
GA The Genuine Article (R) Number: 141HN
TI Rapid assessment of replication error phenotype in gastric cancer
AU Buonsanti G; Presciuttini S; Radice P; Pierotti M A; Bertario L; Ranzani G N (Reprint)
CS UNIV PAVIA, DIPARTIMENTO GENET & MICROBIOL, VIA ABBIATEGRASSO 207, I-27100 PAVIA, ITALY (Reprint); UNIV PAVIA, DIPARTIMENTO GENET & MICROBIOL, I-27100 PAVIA, ITALY; UNIV PISA, DIPARTIMENTO SCI AMBIENTE & TERR, PISA, ITALY; IST NAZL STUDIO & CURA TUMORI, I-20133 MILAN, ITALY
CYA ITALY
SO DIAGNOSTIC MOLECULAR PATHOLOGY, (JUN 1998) Vol. 7, No. 3, pp. 168-173.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 1052-9551.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Forty gastric tumors were investigated for microsatellite instability at the D2S119 and L-myc loci. These tumors and 143 other gastrointestinal cancers were previously analyzed for instability at several different microsatellites. By evaluating previous and present results, repeated sequences were selected that frequently underwent replication errors (RERs). To coamplify these sequences, the following multiplex polymerase chain reactions (PCRs) were performed: 1) D2S119/L-myc/**D18S59**; 2) D2S119/L-myc/D3S1076; and 3) D2S177/L-myc/BAT-RII. Therefore, the 40 gastric tumors in the present survey were rescreened using multiplex PCRs. Each multiplex allowed detection of nearly all RER+ tumors (80% for multiplex 3 and 87% for multiplexes 1 and 2) that had been

previously identified by amplifying 9 different loci with independent reactions. Moreover, for multiplexes 1 and 2, the size differences between normal and RER alleles were sufficient to be detected by electrophoresis on conventional polyacrylamide gels after DNA staining with ethidium bromide. This approach allows a rapid and easy assessment of RER phenotype in gastric tumors.

L29 ANSWER 4 OF 5 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:552930 SCISEARCH
GA The Genuine Article (R) Number: ZZ726
TI Evidence that a locus for familial high myopia maps to chromosome 18p
AU Young T L (Reprint); Ronan S M; Drahozal L A; Wildenberg S C; Alvear A B; Oetting W S; Atwood L D; Wilkin D J; King R A
CS UNIV MINNESOTA, DEPT OPHTHALMOL, BOX 493, 420 DELAWARE ST, MINNEAPOLIS, MN 55455 (Reprint); UNIV MINNESOTA, DEPT MED, MINNEAPOLIS, MN 55455; UNIV MINNESOTA, INST HUMAN GENET, MINNEAPOLIS, MN 55455; UNIV MINNESOTA, DIV EPIDEMIOL, MINNEAPOLIS, MN 55455; NIH, MED GENET BRANCH, NATL HUMAN GENOME RES INST, BETHESDA, MD
CYA USA
SO AMERICAN JOURNAL OF HUMAN GENETICS, (JUL 1998) Vol. 63, No. 1, pp. 109-119.
Publisher: UNIV CHICAGO PRESS, 5720 S WOODLAWN AVE, CHICAGO, IL 60637.
ISSN: 0002-9297.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Myopia, or nearsightedness, is the most common human eye disorder. A genomewide screen was conducted to map the gene(s) associated with high, early-onset, autosomal dominant myopia. Eight families that each included two or more individuals with greater than or equal to-6.00 diopters (D) myopia, in two or more successive generations, were identified. Myopic individuals had no clinical evidence of connective-tissue abnormalities, and the average age at diagnosis of myopia was 6.8 years. The average spherical component refractive error for the affected individuals was -9.48 D. The families contained 82 individuals; of these, DNA was available for 71 (37 affected). Markers nanking or intragenic to the genes for Stickler syndrome types 1 and 2 (chromosomes 12q13.1-q13.3 and 6p21.3, respectively), Marfan syndrome (chromosome 15q21.1), and juvenile glaucoma (chromosome 1q21-q31) were also analyzed. No evidence of linkage was found for markers for the Stickler syndrome types 1 and 2, the Marfan syndrome, or the juvenile glaucoma loci. After a genomewide search, evidence of significant linkage was found on chromosome 18p. The maximum LOD score was 9.59, with marker

D18S481, at a recombination fraction of .0010. Haplotype analysis further refined this myopia locus to a 7.6-cM interval between markers **D18S59** and D18S1138 on 18p11.31.

L29 ANSWER 5 OF 5 MEDLINE
AN 97417341 MEDLINE
DN 97417341
TI A patient with Edwards syndrome caused by a rare pseudodicentric chromosome 18 of paternal origin.
AU Gravholt C H; Bugge M; Stromkjaer H; Caprani M; Henriques U; Petersen M B; Brandt C A
CS Department of Biological Psychiatry, Institute for Basic Research, Psychiatric Hospital in Aarhus, Risskov, Denmark.. cg@afdm.aau.dk
SO CLINICAL GENETICS, (1997 Jul) 52 (1) 56-60.
Journal code: DDT. ISSN: 0009-9163.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
EW 19971201
AB We present an unusual case of trisomy 18 due to a pseudodicentric chromosome 18 of paternal origin. The karyotype was: 46,XY, -18, +psu dic(18)(qter-->cen-->p11.31::p11.31-->psucen-->qter). The origin of the abnormal chromosome was verified by FISH with a painting probe from chromosome 18. Absence of short-arm telomeres was shown by multicolor FISH, and the results of DNA analysis showed monosomy for loci **D18S59** and D18S170 as well as paternal inheritance of the aberrant chromosome. The child's phenotype was characteristic of trisomy 18.

(FILE 'MEDLINE' ENTERED AT 14:34:23 ON 05 MAR 1999)

=> d que l37; d que l39

L30	1595	SEA FILE=MEDLINE ABB=ON	PLU=ON	"AFFECTIVE DISORDERS, PSYCHOTIC"/CT
L31	3290	SEA FILE=MEDLINE ABB=ON	PLU=ON	"MOOD DISORDERS"/CT
L32	13182	SEA FILE=MEDLINE ABB=ON	PLU=ON	"BIPOLAR DISORDER"/CT
L33	1807	SEA FILE=MEDLINE ABB=ON	PLU=ON	"CHROMOSOMES, HUMAN, PAIR 18"/CT
L34	55	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L30 OR L31 OR L32) AND L33
L35	9636	SEA FILE=MEDLINE ABB=ON	PLU=ON	MUTAGENESIS/CT
L36	26031	SEA FILE=MEDLINE ABB=ON	PLU=ON	"POLYMORPHISM (GENETICS)"/CT
L37	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L34 AND (L35 OR L36)

L30	1595	SEA FILE=MEDLINE ABB=ON	PLU=ON	"AFFECTIVE DISORDERS, PSYCHOTIC"/CT	
L31	3290	SEA FILE=MEDLINE ABB=ON	PLU=ON	"MOOD DISORDERS"/CT	
L32	13182	SEA FILE=MEDLINE ABB=ON	PLU=ON	"BIPOLAR DISORDER"/CT	
L33	1807	SEA FILE=MEDLINE ABB=ON	PLU=ON	"CHROMOSOMES, HUMAN, PAIR 18"/CT	
L34	55	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L30 OR L31 OR L32) AND L33	
L38	162916	SEA FILE=MEDLINE ABB=ON	PLU=ON	G5.632./CT ← mutation	
L39	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	L34 AND L38	

=> d 137 .beverlymed

L37 ANSWER 1 OF 1 MEDLINE
AN 97040879 MEDLINE
TI Linkage disequilibrium analysis of G-olf alpha (GNAL) in bipolar affective disorder.
AU Tsiouris S J; Breschel T S; Xu J; McInnis M G; McMahon F J
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1996 Sep 20) 67 (5) 491-4. Journal code: 3L4. ISSN: 0148-7299.
AB This study examines G-olf alpha as a possible candidate gene for susceptibility to bipolar affective disorder (BPAD) using the Transmission Disequilibrium Test (TDT). G-olf alpha, which encodes a subunit of a G-protein involved in intracellular signaling, maps within a region of chromosome 18 that has been implicated by two different linkage studies as a potential site of BPAD susceptibility loci. The expression pattern of G-olf alpha in the brain, its coupling to dopamine receptors, and the effects of lithium salts on G-proteins all support G-olf alpha as a candidate gene for BPAD. Our study population consisted of 106 probands and sibs with bipolar I disorder, with a median age-at-onset of 21.5 years ascertained from the United States. There was no evidence of linkage disequilibrium between BPAD and any of the observed G-olf alpha alleles in our sample. Division of families based on sex of the transmitting parent did not significantly change the results. This sample had good power (78%) to detect linkage disequilibrium with alleles conferring a relative risk equal to that estimated for the putative 18p locus (2.58). Our results do not support a major role for G-olf alpha as a susceptibility locus for BPAD in a substantial portion of our sample. Other genes lying near G-olf alpha within the linked region on chromosome 18 cannot be excluded by our data. This study illustrates the use of the TDT in evaluating candidate genes within linked chromosome regions.

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT' ENTERED AT 14:39:27 ON 05 MAR 1999

L40	272	S FREIMER N?/AU	← Author(s)
L41	0	S SANDUIJL L?/AU	

Searcher : Shears 308-4994

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L42          842 S LEON P?/AU
L43          356 S REUS V?/AU
L44           52 S ESCAMILLA M?/AU
L45          137 S MCINNES L?/AU
L46           91 S SERVICE S?/AU
L47          373 S SANDKUIJL L?/AU
L48           16 S L40 AND L47 AND L42 AND L43 AND L44 AND L45 AND L46
L49           86 S L40 AND (L47 OR L42 OR L43 OR L44 OR L45 OR L46)
L50           30 S L47 AND (L42 OR L43 OR L44 OR L45 OR L46)
L51           35 S L42 AND (L43 OR L44 OR L45 OR L46)
L52           40 S L43 AND (L44 OR L45 OR L46)
L53           27 S L44 AND (L45 OR L46)
L54           22 S L45 AND L46
L55           83 S (L40 OR L47 OR L42 OR L43 OR L44 OR L45 OR L46 OR L49) AND (L1 OR L2 OR
L5)
L56           92 S L48 OR L50 OR L51 OR L52 OR L53 OR L54 OR L55
                 SAV TEMP L56 ARTH976/A

=> fil hom

FILE 'HOME' ENTERED AT 15:00:42 ON 05 MAR 1999

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS,
     CONFSCI, SCISEARCH, JICST-EPLUS, PROMT' ENTERED AT 15:02:25 ON 05
     MAR 1999
                 ACT ARTH976/A
                 ---------

L1   (        272)SEA ABB=ON  PLU=ON  FREIMER N?/AU
L2   (        842)SEA ABB=ON  PLU=ON  LEON P?/AU
L3   (        356)SEA ABB=ON  PLU=ON  REUS V?/AU
L4   (         52)SEA ABB=ON  PLU=ON  ESCAMILLA M?/AU
L5   (        137)SEA ABB=ON  PLU=ON  MCINNES L?/AU
L6   (         91)SEA ABB=ON  PLU=ON  SERVICE S?/AU
L7   (        373)SEA ABB=ON  PLU=ON  SANDKUIJL L?/AU
L8   (         16)SEA ABB=ON  PLU=ON  L1 AND L7 AND L2 AND L3 AND L4 AND
                    L5 AND L6
L9(           86)SEA L1 AND (L7 OR L2 OR L3 OR L4 OR L5 OR L6)
L10(          30)SEA L7 AND (L2 OR L3 OR L4 OR L5 OR L6)
L11(          35)SEA L2 AND (L3 OR L4 OR L5 OR L6)
L12(          40)SEA L3 AND (L4 OR L5 OR L6)
L13(          27)SEA L4 AND (L5 OR L6)
L14(          22)SEA L5 AND L6
L15(          83)SEA (L1 OR L7 OR L2 OR L3 OR L4 OR L5 OR L6 OR L***
L16           92 SEA ABB=ON  PLU=ON  L8 OR L10 OR L11 OR L12 OR L13 OR
L17           50 DUP REM L16 (42 DUPLICATES REMOVED)

L17  ANSWER 1 OF 50  CAPLUS  COPYRIGHT 1999 ACS
AN   1999:90548  CAPLUS
TI   Methods and compositions for the diagnosis and treatment of
                                  Searcher  :  Shears   308-4994
```

neuropsychiatric disorders
IN Chen, Hong; **Freimer, Nelson B.**
PA Millennium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904825	A1	19990204	WO 98-US15183	19980722

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 97-898082 19970722
AB The present invention relates to the mammalian fsh05 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh05 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh05 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh05 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh05 and to using such compds. as therapeutic agents in the treatment of fsh05 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh05 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L17 ANSWER 2 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 1
AN 1998:672566 CAPLUS
DN 129:286742
TI Fsh16 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
IN Chen, Hong; **Freimer, Nelson B.**
PA Millenium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842726	A1	19981001	WO 98-US6210	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9867867	A1	19981020	AU 98-67867	19980327
PRAI	US 97-828009	19970327			
	WO 98-US6210	19980327			

AB The present invention relates to the mammalian fsh16 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh16 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh16 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh16 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh16 and to using such compds. as therapeutic agents in the treatment of fsh16 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh16 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L17 ANSWER 3 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 2
AN 1998:672564 CAPLUS
DN 129:271555
TI Fsh15w6 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
IN Chen, Hong; **Freimer, Nelson B.**
PA Millenium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842724	A1	19981001	WO 98-US6211	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5866412	A	19990202	US 97-828007	19970327

AU 9867868 A1 19981020 AU 98-67868 19980327
PRAI US 97-828007 19970327
WO 98-US6211 19980327
AB The present invention relates to the mammalian fsh15w6 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh15w6 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh15w6 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh15w6 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh15w6 and to using such compds. as therapeutic agents in the treatment of fsh15w6 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh15w6 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L17 ANSWER 4 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 3
AN 1998:672563 CAPLUS
DN 129:286740
TI Fsh22 gene and methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
IN Chen, Hong; **Freimer, Nelson B.**
PA Millenium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842723	A1	19981001	WO 98-US6209	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9867866	A1	19981020	AU 98-67866	19980327

PRAI US 97-828008 19970327
WO 98-US6209 19980327
AB The present invention relates to the mammalian fsh22 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh22 nucleic acids, recombinant DNA mols., cloned genes

or degenerate variants thereof, fsh22 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh22 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh22 and to using such compds. as therapeutic agents in the treatment of fsh22 disorders and neuropsychiatric disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh22 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder**, and to methods and compns. for the treatment of these **disorders**.

L17 ANSWER 5 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 4
AN 1998:672479 CAPLUS
DN 129:287565
TI Methods and compositions for the diagnosis and treatment of neuropsychiatric disorders
IN Chen, Hong; **Freimer, Nelson B.**
PA Millenium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842362	A1	19981001	WO 98-US6208	19980327
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9867865	A1	19981020	AU 98-67865	19980327
PRAI	US 97-828010		19970327		
	WO 98-US6208		19980327		

AB The present invention relates to the mammalian fsh05 gene, a novel gene assocd. with **bipolar affective disorder** (**BAD**) in humans. The invention encompasses fsh05 nucleic acids, recombinant DNA mols., cloned genes or degenerate variants thereof, fsh05 gene products and antibodies directed against such gene products, cloning vectors contg. mammalian fsh05 gene mols., and hosts that have been genetically engineered to express such mols. The invention further relates to methods for the identification of compds. that modulate the expression of fsh05 and to using such compds. as therapeutic agents in the treatment of fsh05 disorders and neuropsychiatric disorders.

The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of fsh05 **disorders** and neuropsychiatric **disorders** including schizophrenia, attention deficit **disorder**, a schizoaffective **disorder**, a **bipolar affective disorder** or a unipolar **affective disorder** , and to methods and compns. for the treatment of these **disorders**.

L17 ANSWER 6 OF 50 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 99-00101 BIOTECHDS
TI New isolated human fsh22 gene; recombinant protein and encoding DNA for use in neuropsychiatric disease diagnosis, therapy and drug screening
AU Chen H; **Freimer N B**
PA Millennium-Pharm.; Univ.California
LO Cambridge, MA, USA; Oakland, CA, USA.
PI WO 9842723 1 Oct 1998
AI WO 98-US6209 27 Mar 1998
PRAI US 97-828008 27 Mar 1997
DT Patent
LA English
OS WPI: 98-542272 [46]
AN 99-00101 BIOTECHDS
AB A nucleic acid molecule (I) encoding a protein of disclosed protein sequence disclosed or encoding a protein encoded by an insert in clone ATCC 98350 is claimed. Also claimed are: nucleic acid hybridizing with the complement of the (I) and encoding a protein involved in a neuropsychiatric disease; (I) which hybridizes under stringent conditions to the complement of (I); a vector containing the disclosed nucleotide sequences; a genetically engineered host cell containing (I); an isolated gene product comprising the disclosed protein sequence or the sequence encoded by the insert of clone ATCC 98350; a gene product encoded by (I); an antibody binding a gene product; a method for therapy of a neuropsychiatric disease in a mammal, which involves administering to the mammal a compound that modulates the synthesis, expression or activity of a mammalian fsh22 gene or gsh22 gene product so that symptoms of the disease are ameliorated; and mapping a human chromosome-18q region spanning DS18S1121 and 18SS30 markers. Gene therapy, transgenic animals, polyclonal, monoclonal, chimeric and humanized antibodies and drug screening are disclosed.

L17 ANSWER 7 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 5
AN 1998:481288 CAPLUS
DN 129:184709
TI Mapping genes for psychiatric disorders and behavioral traits
AU **Mcinnes, L. Alison; Reus, Victor I.**; Freimer, Nelson B.

CS Neurogenetics Laboratory, San Francisco, CA, 94117, USA
SO Curr. Opin. Genet. Dev. (1998), 8(3), 287-292
CODEN: COGDET; ISSN: 0959-437X
PB Current Biology Ltd.
DT Journal; General Review
LA English
AB A review with several refs. In the past year, findings from genetic studies in non-human organisms have yielded a no. of exciting insights regarding the genetic basis of complex behaviors. Although there were encouraging developments in the genetic study of human behavioral traits, particularly those involved with cognitive function, there was relatively little progress in genetic mapping of the most common psychiatric phenotypes.

L17 ANSWER 8 OF 50 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1998251907 EMBASE
TI Chromosome 18 workshop.
AU Van Broeckhoven C.; Verheyen G.; Aita V.M.; Cichon S.; Craddock N.; DeLisi L.E.; **Escamilla M.A.**; Esterling L.E.; Ewald H.; Levinson D.F.; MacKinnon D.F.; **McInnes L.A.**; Merette C.; Murphy V.; Owen M.; Shaw S.H.; Straub R.E.; Turecki G.; Wildenauer D.B.
CS C. Van Broeckhoven, Neurogenetics Laboratory, University of Antwerp, Department of Biochemistry, Antwerp, Belgium
SO Psychiatric Genetics, (1998) 8/2 (97-108).
Refs: 39
ISSN: 0955-8829 CODEN: PSGEEX
CY United Kingdom
DT Journal; Conference Article
FS 005 General Pathology and Pathological Anatomy
022 Human Genetics
032 Psychiatry
LA English

L17 ANSWER 9 OF 50 MEDLINE
AN 97342900 MEDLINE
DN 97342900
TI Understanding the genetic basis of mood disorders: where do we stand? [comment].
CM Comment on: Am J Hum Genet 1997 Jun;60(6):1265-75
AU **Reus V I; Freimer N B**
CS Department of Psychiatry, University of California, San Francisco 94143-0984, USA.. vir@itsa.ucsf.edu
SO AMERICAN JOURNAL OF HUMAN GENETICS, (1997 Jun) 60 (6) 1283-8. Ref: 40
Journal code: 3IM. ISSN: 0002-9297.
CY United States
DT Commentary
Journal; Article; (JOURNAL ARTICLE)

vasopressin; well-developed systems exist for the distribution of vasopressin throughout the CNS via either peptidergic neurons or the CSF and provide the means by which vasopressin may regulate cells controlling behavioral or physiological processes. Among the processes which vasopressin can influence are several of significance in the symptom-complex of affective illness, including alterations in memory, changes in pain sensitivity, synchronization of biological rhythms, the timing and quality of REM [rapid eye movement] sleep, and the regulation of fluid and electrolyte balance. Vasopressin is functionally linked to monoamine neurotransmitter systems and, like them, is altered by pharmacological agents which affect mood. Some of the pharmacological and clinical data suggest that vasopressin function is diminished in depression and augmented in mania; sometimes, however, alterations in vasopressin function may be detectable only during crucial periods of the manic-depressive cycle. The hypothesis that vasopressin plays a role in disorders of human behavior, particularly manic-depressive illness, can now be directly tested by radioimmunoassays of vasopressin in CSF and plasma and by the administration of specific vasopressin analogs and inhibitors.

=> fil hom

FILE 'HOME' ENTERED AT 15:04:25 ON 05 MAR 1999

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199709

L17 ANSWER 10 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 6
AN 1997:679203 CAPLUS
DN 127:327441
TI Methods for detecting **bipolar** mood **disorder** susceptibility locus on human chromosome 18q
IN Friemer, Nelson B.; **Leon, Pedro; Reus, Victor I.** ; **Sandkuijl, Lodewijk A.**; Barondes, Samuel H.
PA Regents of the University of California, USA; Friemer, Nelson B.; Leon, Pedro; Reus, Victor I.; Sandkuijl, Lodewijk A.; Barondes, Samuel H.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9737043	A1	19971009	WO 97-US4904	19970327
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9724238	A1	19971022	AU 97-24238	19970327
	WO 9807887	A1	19980226	WO 97-US14892	19970822
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9741604	A1	19980306	AU 97-41604	19970822
PRAI	US 96-14498		19960329		
	US 96-23438		19960823		
	WO 97-US4904		19970327		
	WO 97-US14892		19970822		

AB The present invention is directed to methods of detecting the

presence of a **bipolar** mood **disorder** susceptibility locus in an individual, comprising analyzing a sample of DNA for the presence of a DNA polymorphism on the long arm of chromosome 18 between markers D18S469 and D18S554, wherein the DNA polymorphism is assocd. with a form of **bipolar** mood **disorder (BP)**. The invention for the first time provides strong evidence of a susceptibility gene for BP that is located in the 18q22-q23 region of the long arm of chromosome 18. The disclosure describes the use of linkage anal. and genetic markers in the 18q22-q23 region to fine map the region and the use of genetic markers to genetically diagnose (genotype) BP in individuals, to confirm phenotypic diagnoses of BP, to det. appropriate treatments for patients with particular genotypic subtypes. Isolated polynucleotides useful for genetic linkage anal. of BP-I and methods for obtaining such isolated polynucleotides are also described. In screening for a BP susceptibility locus, only those individuals with the most severe and clin. distinctive form of BP were considered as affected. Two large pedigrees were selected from a genetically homogeneous population, that of the Central Valley of Costa Rica. The entire human genome was screened for linkage using mapped microsatellite markers and a model for genetic anal. in which most of the linkage information derived from affected individuals. Three lines of evidence supported the localization of a BP susceptibility locus to 18q22-q23: assocn. anal., linkage anal., and direct observation of a conserved marker haplotype.

L17 ANSWER 11 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:76133 SCISEARCH
GA The Genuine Article (R) Number: YQ995
TI Population based genetic mapping of **bipolar disorder (BP)** in Costa Rica
AU **Escamilla M A (Reprint)**; **McInnes L A**; Spesny M; **Reus V I**; **Service S**; Shimayoshi N; Tyler D; Batki S; Vinogradov S; Neylan T; Molina J; Meza L; Gallegos A; Mendez R; Fournier E; Mathews C; Emch D; DeMille M; **Leon P**; Roche E; Silva S; **Sandkuijl L**; **Freimer N B**
CS UNIV CALIF SAN FRANCISCO, DEPT PSYCHIAT, CTR NEUROBIOL & PSYCHIAT, SAN FRANCISCO, CA 94143; UNIV COSTA RICA, SAN JOSE, COSTA RICA; ERASMUS UNIV ROTTERDAM, NL-3000 DR ROTTERDAM, NETHERLANDS; LEIDEN UNIV, NL-2300 RA LEIDEN, NETHERLANDS
CYA USA; COSTA RICA; NETHERLANDS
SO AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 1997) Vol. 61, No. 4, Supp. [S], pp. 1598-1598.
Publisher: UNIV CHICAGO PRESS, 5720 S WOODLAWN AVE, CHICAGO, IL 60637.
ISSN: 0002-9297.
DT Conference; Journal
FS LIFE; CLIN
LA English

REC Reference Count: 0

L17 ANSWER 12 OF 50 LIFESCI COPYRIGHT 1999 CSA DUPLICATE 7
AN 1998:15789 LIFESCI
TI Understanding the genetic basis of mood disorders: Where do we stand?
AU **Reus, V.I.; Freimer, N.B.**
CS Center for Neurobiology and Psychiatry, Department of Psychiatry, University of California, San Francisco, 401 Parnassus Avenue, San Francisco, CA 94143-0984, USA
SO AM. J. HUM. GENET., (19970600) vol. 60, no. 6, pp. 1283-1288. ISSN: 0002-9297.
DT Journal
TC General Review
FS G; N3
LA English
SL English
AB In this issue of the Journal, Sherman et al. describe the promise of genetic approaches for understanding human behavior and point out a number of obstacles to realization of this promise; these include the methodological challenge of identifying genes for complex traits and the societal challenge of appropriately using the information that will be gained if such genetic-mapping efforts are successful. Genetic-mapping studies in humans rest on the premise that traits of interest can be reduced to one or more discrete phenotypes and that these phenotypes result, at least in part, from particular alleles at susceptibility loci of reasonably large effect. As discussed in this review, abundant evidence suggests that severe **bipolar** mood **disorder** (**BP**) fulfills this premise better than other human behavioral traits. The diagnosis of **BP** is highly reliable, and its delineation as a distinct syndrome has proved to be clinically useful in predicting course and response to treatment. However, one must keep in mind that this diagnostic category, like all psychiatric classifications, is based on operational criteria (derived from a combination of epidemiological and clinical observations), rather than on any anatomical or physiological evidence. This fact differentiates psychiatric **disorders** from other etiologically complex categories of **disease**, such as hypertension or diabetes mellitus. In this review we discuss our current understanding of the genetic basis of **BP** and other mood **disorders** and indicate how our body of knowledge has been influenced by different approaches to the definition of **disease** phenotypes.

L17 ANSWER 13 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:852348 SCISEARCH
GA The Genuine Article (R) Number: YB414
TI Fine mapping of a locus for severe **bipolar** mood **disorder** in the Costa Rican population using linkage

disequilibrium methods.

AU **McInnes L A (Reprint)**; Barnes G T; Barondes S; Batki S; Chen H; Charlat O; Crook S; Duyk G M; **Escamilla M E**; Fournier E; Gallegos A; Gajiwala P; Gitt M; Jawalar S; **Leon P**; Luo D; Matthews C; Meza L; Molina J; Neylan T; **Sandkuijl L**; **Service S K**; Silva S; Spesny M; **Reus V I**; Roche E; Rojas E; **Freimer N B**

CS UNIV CALIF SAN FRANCISCO, DEPT PSYCHIAT, CTR NEUROBIOL & PSYCHIAT, SAN FRANCISCO, CA 94143; MILLENNIUM PHARMACEUT, CAMBRIDGE, MA; UNIV CALIF SAN FRANCISCO, SAN FRANCISCO GEN HOSP, SAN FRANCISCO, CA; UNIV COSTA RICA, CELL & MOL BIOL RES CTR, SAN JOSE, COSTA RICA; UNIV COSTA RICA, ESCUELA MED, SAN JOSE, COSTA RICA; HOSP CALDERON GUARDIA, SAN JOSE, COSTA RICA; ERASMUS UNIV ROTTERDAM, DEPT CLIN GENET, NL-3000 DR ROTTERDAM, NETHERLANDS; LEIDEN UNIV, DEPT HUMAN GENET, NL-2300 RA LEIDEN, NETHERLANDS; UNIV GRONINGEN, DEPT MED GENET, NL-9700 AB GRONINGEN, NETHERLANDS; UNIV CALIF SAN FRANCISCO, GENET PROGRAM, SAN FRANCISCO, CA 94143; UNIV CALIF SAN FRANCISCO, PROGRAM BIOMED SCI, SAN FRANCISCO, CA 94143

CYA USA; COSTA RICA; NETHERLANDS

SO AMERICAN JOURNAL OF MEDICAL GENETICS, (21 NOV 1997) Vol. 74, No. 6, pp. 674-674.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0148-7299.

DT Conference; Journal

FS LIFE

LA English

REC Reference Count: 0

L17 ANSWER 14 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)

AN 97:852342 SCISEARCH

GA The Genuine Article (R) Number: YB414

TI Linkage disequilibrium analysis of **bipolar disorder** in the Costa Rican population.

AU **Escamilla M A (Reprint)**; **McInnes L A**; Spesny M; **Reus V I**; Shimayoshi N; Tyler D; Batki S; Vinogrado S; Neylan T; Meza L; Gallegos A; Fournier E; Emch D; DeMille M; **Leon P**; **Service S**; Roche E; Silva S; **Sandkuijl L**; **Freimer N B**

CS UNIV CALIF SAN FRANCISCO, DEPT PSYCHIAT, CTR NEUROBIOL & PSYCHIAT, SAN FRANCISCO, CA 94143; ERASMUS UNIV ROTTERDAM, ROTTERDAM, NETHERLANDS; LEIDEN UNIV, NL-2300 RA LEIDEN, NETHERLANDS

CYA USA; NETHERLANDS

SO AMERICAN JOURNAL OF MEDICAL GENETICS, (21 NOV 1997) Vol. 74, No. 6, pp. 672-672.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0148-7299.

DT Conference; Journal

FS LIFE
LA English
REC Reference Count: 0

L17 ANSWER 15 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:852265 SCISEARCH
GA The Genuine Article (R) Number: YB414
TI Linkage disequilibrium mapping of schizophrenia in the Costa Rican population.
AU **Escamilla M A (Reprint)**; Raventos H; Montero P; Vinogradov S; Armas R; **Reus V I**; Gallegos A; Badilla R; Molina J
CS UNIV CALIF SAN FRANCISCO, DEPT PSYCHIAT, CTR NEUROBIOL & PSYCHIAT, SAN FRANCISCO, CA 94143; UNIV COSTA RICA, ESCUELA MED, SAN JOSE, COSTA RICA
CYA USA; COSTA RICA
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (21 NOV 1997) Vol. 74, No. 6, pp. 650-650.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0148-7299.
DT Conference; Journal
FS LIFE
LA English
REC Reference Count: 0

L17 ANSWER 16 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:111519 BIOSIS
DN PREV19980111519
TI Population based genetic mapping of **bipolar disorder (BP)** in Costa Rica.
AU **Escamilla, M. A. (1)**; **McInnes, L. A. (1)**; Spesny, M.; **Reus, V. I. (1)**; **Service, S. (1)**; Shimayoshi, N. (1); Tyler, D. (1); Batki, S. (1); Vinogradov, S. (1); Neylan, T. (1); Molina, J.; Meza, L.; Gallegos, A.; Mendez, R.; Fournier, E.; Mathews, C. (1); Emch, D. (1); Demille, M. (1); **Leon, P.**; Roche, E. (1); Silva, S.; **Sandkuijl, L.**; **Freimer, N. B. (1)**
CS (1) Center Neurobiol. and Psychiatry, Dep. Psychiatry, Univ. California at San Francisco, San Francisco, CA USA
SO American Journal of Human Genetics, (Oct., 1997) Vol. 61, No. 4 SUPPL., pp. A274.
Meeting Info.: 47th Annual Meeting of the American Society of Human Genetics Baltimore, Maryland, USA October 28-November 1, 1997
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 17 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 8
AN 1996:689777 CAPLUS

DN 126:5800
TI A complete genome screen for genes predisposing to severe **bipolar disorder** in two Costa Rican pedigrees
AU **McInnes, L. Alison; Escamilla, Michael A.; Service, Susan K.; Reus, Victor I.; Leon, Pedro;** Silva, Sandra; Rojas, Eugenia; Spesny, Mitzi; Baharloo, Siamak; et al.
CS Neurogenet. Lab., Univ. California, San Francisco, CA, 94143, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(23), 13060-13065
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB **Bipolar** mood **disorder (BP)** is a debilitating syndrome characterized by episodes of mania and depression. We designed a multistage study to detect all major loci predisposing to severe BP (termed BP-I) in two pedigrees drawn from the Central Valley of Costa Rica, where the population is largely descended from a few founders in the 16th-18th centuries. We considered only individuals with BP-I as affected and screened the genome for linkage with 473 microsatellite markers. We used a model for linkage anal. that incorporated a high phenocopy rate and a conservative est. of penetrance. Our goal in this study was not to establish definitive linkage but rather to detect all regions possibly harboring major genes for BP-I in these pedigrees. To facilitate this aim, we evaluated the degree to which markers that were informative in our data set provided coverage of each genome region; we est. that at least 94% of the genome has been covered, at a predesignated threshold detd. through prior linkage simulation analyses. We report here the results of our genome screen for BP-I loci and indicate several regions that merit further study, including segments in 18q, 18p, and 11p, in which suggestive lod scores were obsd. for two or more contiguous markers. Isolated lod scores that exceeded our thresholds in one or both families also occurred on chromosomes 1, 2, 3, 4, 5, 7, 13, 15, 16, and 17. Interesting regions highlighted in this genome screen will be followed up using linkage disequil (LD) methods.

L17 ANSWER 18 OF 50 LIFESCI COPYRIGHT 1999 CSA
AN 97:38966 LIFESCI
TI A complete genome screen for genes predisposing to severe **bipolar disorder** in two Costa Rican pedigrees
AU **McInnes, L.A.; Escamilla, M.A.; Service, S.K.; Reus, V.I.; Leon, P.;** Silva, S.; Rojas, E.; Spesny, M.; **Freimer, N.B.***; et al.
CS Univ. California, Box F-0984, San Francisco, CA 94143, USA
SO PROC. NATL. ACAD. SCI. USA, (1996) vol. 93, no. 24, pp. 13060-13065. ISSN: 0027-8424.
DT Journal

Searcher : Shears 308-4994

FS G; N3
LA English
SL English
AB **Bipolar** mood **disorder** (**BP**) is a debilitating syndrome characterized by episodes of mania and depression. We designed a multistage study to detect all major loci predisposing to severe **BP** (termed **BP**-I) in two pedigrees drawn from the Central Valley of Costa Rica, where the population is largely descended from a few founders in the 16th-18th centuries. We considered only individuals with **BP**-I as affected and screened the genome for linkage with 473 microsatellite markers. We used a model for linkage analysis that incorporated a high phenocopy rate and a conservative estimate of penetrance. Our goal in this study was not to establish definitive linkage but rather to detect all regions possibly harboring major genes for **BP**-I in these pedigrees. To facilitate this aim, we evaluated the degree to which markers that were informative in our data set provided coverage of each genome region; we estimate that at least 94% of the genome has been covered, at a predesignated threshold determined through prior linkage simulation analyses. We report here the results of our genome screen for **BP**-I loci and indicate several regions that merit further study, including segments in 18q, 18p, and 11p, in which suggestive lod scores were observed for two or more contiguous markers. Isolated lod scores that exceeded our thresholds in one or both families also occurred on chromosomes 1, 2, 3, 4, 5, 7, 13, 15, 16, and 17. Interesting regions highlighted in this genome screen will be followed up using linkage disequilibrium (LD) methods.

L17 ANSWER 19 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 96:891440 SCISEARCH
GA The Genuine Article (R) Number: VV138
TI Additional support for schizophrenia linkage on chromosomes 6 and 8: A multicenter study
AU Levinson D F (Reprint); Wildenauer D B; Schwab S G; Albus M; Hallmayer J; Lerer B; Maier W; Blackwood D; Muir W; StClair D; Morris S; Moises H W; Yang L; Kristbjarnarson H; Helgason T; Wiese C; Collier D A; Holmans P; Daniels J; Rees M; Asherson P; Roberts Q; Cardno A; Arranz M J; Vallada H; McGuffin D; Owen M J; Pulver A E; Antonarakis S E; Babb R; Blouin J L; DeMarchi N; Dombroski B; Housman D; Karayiorgou M; Ott J; Kasch L; Kazazian H; Lasseter V K; Loetscher E; Luebbert H; Nestadt G; Ton C; Wolyniec P S; Laurent C; deChaldee M; Thibaut F; Jay M; Samolyk D; Petit M; Campion D; Mallet J; Straub R E; MacLean C J; Easter S M; ONeill F A; Walsh D; Kendler K S; Gejman P V; Cao Q H; Gershon E; Badner J; Beshah E; Zhang J; Riley B P; Rajagopalan S; MogudiCarter M; Jenkins T; Williamson R; DeLisi L E; Garner C; Kelly M; LeDuc C; Cardon L; Lichter J; Harris T; Loftus J; Shields G; Comasi M; Vita A; Smith A; Dann J; Joslyn G; Gurling H; Kalsi G; Brynjolfsson J; Curtis D; Sigmundsson T; Butler

R; Read T; Murphy P; Chen A C H; Petursson H; Byerley B; Hoff M; Holik J; Coon H; Nancarrow D J; Crowe R R; Andreasen N; Silverman J M; Mohs R C; Siever L J; Endicott J; Sharpe L; Walters M K; Lennon D P; Hayward N K; **Sandkuijl L A**; Mowry B J; Aschauer H N; Meszaros K; Lenzinger E; Fuchs K; Heiden A M; Kruglyak L; Daly M J; Matise T C

CS UNIV BONN, DEPT PSYCHIAT, D-5300 BONN, GERMANY (Reprint); STATE MENTAL HOSP, HAAR, GERMANY; UNIV WESTERN AUSTRALIA, GRAYLANDS UWA CLIN RES UNIT, PERTH, WA 6009, AUSTRALIA; HEBREW UNIV JERUSALEM, HADASSAH MED CTR, DEPT PSYCHIAT, JERUSALEM, ISRAEL; UNIV EDINBURGH, ROYAL EDINBURGH HOSP, DEPT PSYCHIAT, EDINBURGH EH8 9YL, MIDLOTHIAN, SCOTLAND; WESTERN GEN HOSP, HUMAN GENET UNIT, MRC, EDINBURGH, MIDLOTHIAN, SCOTLAND; NATL UNIV HOSP, DEPT PSYCHIAT, REYKJAVIK, ICELAND; UNIV KIEL KLINIKUM, DEPT PSYCHIAT, KIEL, GERMANY; INST PSYCHIAT, DEPT PSYCHOL MED, MOL GENET SECT, LONDON SE5 8AF, ENGLAND; INST PSYCHIAT, DEPT NEUROPATHOL, MOL GENET SECT, LONDON SE5 8AF, ENGLAND; UNIV WALES COLL MED, DEPT PSYCHOL MED, CARDIFF CF4 4XN, S GLAM, WALES; UNIV WALES COLL MED, DEPT MED GENET, CARDIFF CF4 4XN, S GLAM, WALES; TEIKYO UNIV, SCH MED, DEPT PSYCHIAT, TOKYO 173, JAPAN; ST JAMES HOSP, TRINITY CTR HLTH SCI, DUBLIN 8, IRELAND; JOHNS HOPKINS UNIV, DEPT PEDIAT, BALTIMORE, MD 21218; JOHNS HOPKINS UNIV, DEPT PSYCHIAT & BEHAV SCI, BALTIMORE, MD 21218; UNIV GENEVA, DEPT GENET, SCH MED, CH-1211 GENEVA 4, SWITZERLAND; UNIV NAPLES 2, INST PSYCHIAT, NAPLES, ITALY; UNIV PENN, MED CTR, DEPT GENET, PHILADELPHIA, PA 19104; MIT, CTR CANC RES, CAMBRIDGE, MA 02139; ROCKEFELLER UNIV, HUMAN NEUROGENET LAB, NEW YORK, NY 10021; ROCKEFELLER UNIV, LAB STAT GENET, NEW YORK, NY 10021; SANDOZ PHARMA LTD, BASEL, SWITZERLAND; HOP LA PITIE SALPETRIERE, LAB GENET MOL NEUROTRANSMISS & PROC NEURODEGENER, CNRS, PARIS, FRANCE; CHS ST PAUL, ST PAUL, REUNION; CHS SOTTEVILLE, ROUEN, FRANCE; VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT PSYCHIAT, RICHMOND, VA 23298; VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT HUMAN GENET, RICHMOND, VA 23298; UNIV QUEENSLAND, DEPT PSYCHIAT, BELFAST, ANTRIM, NORTH IRELAND; HLTH RES BOARD, DUBLIN, IRELAND; NIMH, CLIN NEUROGENET BRANCH, BETHESDA, MD 20892; ST MARYS HOSP, SCH MED, DEPT BIOCHEM & MOL GENET, LONDON W2 1PG, ENGLAND; BARAGWANATH HOSP, DEPT PSYCHIAT, SOWETO, SOUTH AFRICA; UNIV WITWATERSRAND, DEPT HUMAN GENET, SCH PATHOL, S AFRICAN INST MED RES, JOHANNESBURG, SOUTH AFRICA; SEQUANA THERAPEUT INC, SAN DIEGO, CA; SUNY STONY BROOK, DEPT PSYCHIAT, STONY BROOK, NY 11794; WARNEFORD HOSP, DEPT PSYCHIAT, OXFORD OX3 7JX, ENGLAND; UNIV MILAN, I-20122 MILAN, ITALY; UNIV COLL LONDON, SCH MED, MOL PSYCHIAT LAB, DEPT PSYCHIAT, LONDON W1N 8AA, ENGLAND; UNIV ICELAND, DEPT PSYCHIAT, BORGARSPITINN, IS-101 REYKJAVIK, ICELAND; LONDON HOSP, COLL MED, DEPT PSYCHOL MED, LONDON, ENGLAND; UNIV UTAH, MED CTR, DEPT PSYCHIAT, SALT LAKE CITY, UT; ALLEGHENY UNIV HLTH SCI, DEPT PSYCHIAT, PHILADELPHIA, PA 19102; UNIV QUEENSLAND, DEPT PSYCHIAT, WOLSTON PK HOSP, BRISBANE, QLD, AUSTRALIA; QUEENSLAND INST MED RES, BRISBANE, QLD 4006, AUSTRALIA; UNIV IOWA, COLL MED, DEPT PSYCHIAT, IOWA CITY, IA 52242; UNIV IOWA,

COLL MED, MENTAL HLTH CLIN RES CTR, IOWA CITY, IA 52242; MT SINAI SCH MED, DEPT PSYCHIAT, NEW YORK, NY; COLUMBIA UNIV, NEW YORK STATE PSYCHIAT INST, NEW YORK, NY; ERASMUS UNIV, DEPT CLIN GENET, NL-3000 DR ROTTERDAM, NETHERLANDS; LEIDEN UNIV, DEPT GENET, NL-2300 RA LEIDEN, NETHERLANDS; UNIV GRONINGEN, DEPT MED GENET, NL-9700 AB GRONINGEN, NETHERLANDS; UNIV VIENNA, HOSP PSYCHIAT, DEPT GEN PSYCHIAT, VIENNA, AUSTRIA; COLUMBIA UNIV COLL PHYS & SURG, DEPT PSYCHIAT, NEW YORK, NY 10032; WHITEHEAD INST BIOMED RES, CAMBRIDGE, MA

CYA GERMANY; AUSTRALIA; ISRAEL; SCOTLAND; ICELAND; ENGLAND; WALES; JAPAN; IRELAND; USA; SWITZERLAND; ITALY; FRANCE; REUNION; NORTH IRELAND; SOUTH AFRICA; NETHERLANDS; AUSTRIA

SO AMERICAN JOURNAL OF MEDICAL GENETICS, (22 NOV 1996) Vol. 67, No. 6, pp. 580-594.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0148-7299.

DT Article; Journal

FS LIFE

LA English

REC Reference Count: 55
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In response to reported schizophrenia linkage findings on chromosomes 3, 6 and 8, fourteen research groups genotyped 14 microsatellite markers in an unbiased, collaborative (New) sample of 403-567 informative pedigrees per marker, and in the Original sample which produced each finding (the Johns Hopkins University sample of 40-52 informative pedigrees for chromosomes 3 and 8, and the Medical College of Virginia sample of 156-191 informative pedigrees for chromosome 6). Primary planned analyses (New sample) were two-point heterogeneity lod score (lod2) tests (dominant and recessive affected-only models), and multipoint affected sibling pair (ASP) analysis, with a narrow diagnostic model schizophrenia and schizoaffective disorders), Regions with positive results were also analyzed in the Original and Combined samples. There was no evidence for linkage on chromosome 3. For chromosome 6, ASP maximum lod scores (MLS) were 2.19 (New sample, nominal p = .001) and. 2.68 (Combined sample, p = .0004). For chromosome 8, maximum lod2 scores (tests of linkage with heterogeneity) were 2.22 (New sample, p = .0014) and 3.06 (Combined sample, p = .00018). Results are interpreted as inconclusive hut suggestive of linkage in the latter two regions. We discuss possible reasons for failing to achieve a conclusive result in this large sample, Design issues and limitations of this type of collaborative study are discussed, and it is concluded that multicenter follow-up linkage studies of complex disorders can help to direct research efforts toward promising regions.

AN 96416031 MEDLINE
DN 96416031
TI Attitudes towards **bipolar disorder** and predictive genetic testing among patients and providers.
AU Smith L B; Sapers B; **Reus V I**; **Freimer N B**
CS Department of Psychiatry, University of California at San Francisco 94143-0984, USA.
NC MH 00916 (NIMH)
MH 49499 (NIMH)
SO JOURNAL OF MEDICAL GENETICS, (1996 Jul) 33 (7) 544-9.
Journal code: J1F. ISSN: 0022-2593.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
AB Attitudes about **bipolar disorder** (manic depressive **disorder**) and genetic testing were investigated. Three groups of subjects were surveyed including members of a manic depressive support group, medical students, and psychiatry residents. The questionnaire was intended to elicit impressions and attitudes about **bipolar disorder** (**BP**) from mental health consumers and health care providers with varying levels of personal and professional familiarity with the **disorder**. Attitudes towards prenatal testing and pregnancy termination were also assessed. The intention hypothetically to terminate a pregnancy was influenced by the likelihood of developing **BP** a well as the projected course and severity of illness. Nearly half of the total sample would terminate pregnancy if the fetus were definitely to develop an unspecified form of **bipolar disorder**. Presumed severity of illness was also found to be a modifying factor in the decision, with a low percentage of subjects electing to terminate for a mild course of **bipolar disorder** and a majority opting for termination in the case of an extremely severe presentation. Support group members were the least likely to terminate a hypothetical pregnancy in the case of a positive prenatal test and were the most likely to desire childhood testing in the absence of preventive or treatment options. The possible implications of these findings, as well as avenues of future research, are discussed.

L17 ANSWER 21 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 10
AN 1996:312108 CAPLUS
DN 125:2666
TI Genetic mapping using haplotype, association and linkage methods suggests a locus for severe **bipolar disorder** (**BPI**) at 18q22-q23
AU **Freimer, Nelson B.**; **Reus, Victor I.**;

Escamilla, Michael A.; McInnes, L. Alison; Spesny, Mitzi; **Leon, Pedro; Service, Susan K.;** Smith, Lauren B.; Silva, Sandra; et al.
CS Neurogenetics Laboratory, Univ. of California San Francisco, San Francisco, CA, 94143, USA
SO Nat. Genet. (1996), 12(4), 436-441
CODEN: NGENEC; ISSN: 1061-4036
DT Journal
LA English
AB Manic-depressive illness, or **bipolar disorder** (**BP**), is characterized by episodes of elevated mood (mania) and depression1. We designed a multistage study in the genetically isolated population of the Central Valley of Costa Rica2,3 to identify genes that promote susceptibility to severe BP (termed BPI), and screened the genome of two Costa Rican BPI pedigrees (McInnes et al., submitted). We considered only individuals who fulfilled very stringent diagnostic criteria for BPI to be affected. The strongest evidence for a BPI locus was obsd. in 18q22-q23. We tested 16 addnl. markers in this region and seven yielded peak lod scores over 1.0. These suggestive lod scores were obtained over a far greater chromosomal length (about 40 cM) than in any other genome region. This localization is supported by marker haplotypes shared by 23 of 26 BPI affected individuals studied. Addnl., marker allele frequencies over portions of this region are significantly different in the patient sample from those of the general Costa Rican population. Finally, we performed an anal. which made use of both the evidence for linkage and for assocn. in 18q23, and we obsd. significant lod scores for two markers in this region.

L17 ANSWER 22 OF 50 MEDLINE DUPLICATE 11
AN 96348620 MEDLINE
DN 96348620
TI An approach to investigating linkage for **bipolar disorder** using large Costa Rican pedigrees.
AU **Freimer N B; Reus V I; Escamilla M;** Spesny M; Smith L; **Service S;** Gallegos A; Meza L; Batki S; Vinogradov S; **Leon P; Sandkuijl L A**
CS Center for Neurobiology and Psychiatry, University of California, San Francisco 94143, USA.
NC MH49499 (NIMH)
MH48695 (NIMH)
MH00916 (NIMH)
+
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1996 May 31) 67 (3) 254-63.
Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

Searcher : Shears 308-4994

EM 199702
EW 19970204
AB Despite the evidence that major gene effects exist for **bipolar disorder** (**BP**), efforts to map **BP** loci have so far been unsuccessful. A strategy for mapping **BP** loci is described, focused on investigation of large pedigrees from a genetically homogenous population, that of Costa Rica. This approach is based on the use of a conservative definition of the **BP** phenotype in preparation for whole genome screening with polymorphic markers. Linkage simulation analyses are utilized to indicate the probability of detecting evidence suggestive of linkage, using these pedigrees. These analyses are performed under a series of single locus models, ranging from recessive to nearly dominant, utilizing both lod score and affected pedigree member analyses. Additional calculations demonstrate that with any of the models employed, most of the information for linkage derives from affected rather than unaffected individuals.

L17 ANSWER 23 OF 50 MEDLINE DUPLICATE 12
AN 96348619 MEDLINE
DN 96348619
TI Use of linkage disequilibrium approaches to map genes for **bipolar disorder** in the Costa Rican population.
AU **Escamilla M A**; Spesny M; **Reus V I**; Gallegos A; Meza L; Molina J; **Sandkuijl L A**; Fournier E; **Leon P E**; Smith L B; **Freimer N B**
CS Department of Psychiatry, University of California at San Francisco 94143, USA.
NC MH 00916 (NIMH)
MH 49499 (NIMH)
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1996 May 31) 67 (3) 244-53. Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB Linkage disequilibrium (LD) analysis provides a powerful means for screening the genome to map the location of **disease** genes, such as those for **bipolar disorder** (**BP**). As described in this paper, the population of the Central Valley of Costa Rica, which is descended from a small number of founders, should be suitable for LD mapping; this assertion is supported by reconstruction of extended haplotypes shared by distantly related individuals in this population suffering low-frequency hearing loss (LFHL1), which has previously been mapped by linkage analysis. A sampling strategy is described for applying LD methods to map genes

for **BP**, and clinical and demographic characteristics of an initially collected sample are discussed. This sample will provide a complement to a previously collected set of Costa Rican **BP** families which is under investigation using standard linkage analysis.

L17 ANSWER 24 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:556289 BIOSIS
DN PREV199699278645
TI A complete genome screen for genes predisposing to severe **bipolar disorder** in two Costa Rican pedigrees.
AU **McInnes, L. A. (1); Escamilla, M. A. (1); Service, S. K. (1); Reus, V. I. (1); Leon, P.**; Silva, S.; Rojas, E.; Spesny, M.; Baharloo, S. (1); Tobey, C. (1); Batki, S. (1); Vinogradov, S. (1); Meza, L.; Gallegos, A.; Fournier, E.; Smith, L. B. (1); Barondes, S. H. (1); **Sandkuijl, L. A.; Freimer, N. B. (1)**
CS (1) Univ. Calif. San Francisco, San Francisco, CA USA
SO American Journal of Human Genetics, (1996) Vol. 59, No. 4 SUPPL., pp. A227.
Meeting Info.: 46th Annual Meeting of the American Society of Human Genetics San Francisco, California, USA October 29-November 2, 1996
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 25 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 95:712605 SCISEARCH
GA The Genuine Article (R) Number: RW687
TI ATTITUDES TOWARD **BIPOLAR DISORDER** AND PREDICTIVE GENETIC TESTING AMONG PATIENTS AND PROVIDERS
AU SMITH L B (Reprint); SAPERS B; **REUS V I; FREIMER N B**
CS UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 00000
CYA USA
SO AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 1995) Vol. 57, No. 4, Supp. S, pp. 1735.
ISSN: 0002-9297.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC No References

L17 ANSWER 26 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 95:712001 SCISEARCH
GA The Genuine Article (R) Number: RW687
TI A COMPLETE GENOME SEARCH FOR GENETIC-LOCI PREDISPOSING TO **BIPOLAR DISORDER** (**BP**) IN 2 COSTA-RICAN PEDIGREES

AU **MCINNES L A (Reprint)**; **ESCAMILLA M A**; **REUS V I**; SPESNY M; **LEON P**; ROJAS E; TYLER D; BAHARLOO S; BLANKENSHIP K; BATKI S; VINOGRADOV S; MEZA L; GALLEGOS A; FOURNIER E; **SERVICE S**; SMITH L; SILVA S; **SANDKUIJL L**; **FREIMER N B**

CS UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 94143; UNIV COSTA RICA, SAN JOSE, COSTA RICA; ERASMUS UNIV ROTTERDAM, ROTTERDAM, NETHERLANDS; LEIDEN UNIV, LEIDEN, NETHERLANDS

CYA USA; COSTA RICA; NETHERLANDS

SO AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 1995) Vol. 57, No. 4, Supp. S, pp. 1134.
ISSN: 0002-9297.

DT Conference; Journal

FS LIFE; CLIN

LA ENGLISH

REC No References

L17 ANSWER 27 OF 50 MEDLINE

AN 96004344 MEDLINE

DN 96004344

TI Mapping genes for psychiatric disorders and behavioral traits.

AU **McInnes L A**; **Freimer N B**

CS Department of Psychiatry, University of California San Francisco 94143, USA..

NC K21 MH00916 (NIMH)
R01 MH49499 (NIMH)
R01 MH47563 (NIMH)

SO CURRENT OPINION IN GENETICS AND DEVELOPMENT, (1995 Jun) 5 (3) 376-81. Ref: 41
Journal code: BJC. ISSN: 0959-437X.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)

LA English

FS Priority Journals

EM 199601

AB In the past year, some of the most exciting findings in the genetic investigation of mammalian behavior have been obtained through mapping and through gene manipulation studies in the mouse system. These include the localization of a gene for circadian periodicity in the mouse, gene knockouts of serotonin receptors, and the development of a transgenic model of Alzheimer's disease. The recent development of genetic maps covering the entire human genome and the implementation of new approaches to genetic analysis may now facilitate elucidation of complex behaviors in humans, particularly psychiatric disorders.

L17 ANSWER 28 OF 50 BIOSIS
Searcher : Shears 308-4994

AN 1995:478057 BIOSIS
DN PREV199598492357
TI Attitudes toward **bipolar disorder** and predictive genetic testing among patients and providers.
AU Smith, L. B.; Sapers, B.; **Reus, V. I.**; **Freimer, N. B.**
CS Univ. Calif., San Francisco, CA USA
SO American Journal of Human Genetics, (1995) Vol. 57, No. 4 SUPPL., pp. A298.
Meeting Info.: 45th Annual Meeting of the American Society of Human Genetics Minneapolis, Minnesota, USA October 24-28, 1995
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 29 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:477456 BIOSIS
DN PREV199598491756
TI A complete genome search for genetic loci predisposing to **bipolar disorder** (**BP**) in two Costa Rican pedigrees.
AU **McInnes, L. A. (1)**; **Escamilla, M. A. (1)**; **Reus, V. I. (1)**; Spesny, M.; **Leon, P.**; Rojas, E.; Tyler, D.; Baharloo, S. (1); Blankenship, K. (1); Batki, S. (1); Vinogradov, S. (1); Meza, L.; Gallegos, A.; Fournier, F.; **Service, S.**; Smith, L. (1); Silva, S.; **Sandkuijl, L.**; **Freimer, N. B. (1)**
CS (1) Univ. Calif. San Francisco, San Francisco, CA USA
SO American Journal of Human Genetics, (1995) Vol. 57, No. 4 SUPPL., pp. A197.
Meeting Info.: 45th Annual Meeting of the American Society of Human Genetics Minneapolis, Minnesota, USA October 24-28, 1995
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 30 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 95:711000 SCISEARCH
GA The Genuine Article (R) Number: RW687
TI LINKAGE DISEQUILIBRIUM ANALYSIS OF **BIPOLAR DISORDER** (**BP**) IN THE COSTA-RICAN POPULATION
AU **ESCAMILLA M A (Reprint)**; **MCINNES L A**; SPESNY M; **REUS V I**; SHIMAYOSHI N; TYLER D; BATKI S; VINOGRADOV S; MEZA L; GALLEGOS A; MOLINA J; FOURNIER E; **LEON P**; **SERVICE S**; SMITH L; SILVA S; **SANDKUIJL L**; **FREIMER N B**
CS UNIV CALIF SAN FRANCISCO, SAN FRANCISCO, CA, 94143; UNIV COSTA RICA, SAN JOSE, COSTA RICA; ERASMUS UNIV ROTTERDAM, ROTTERDAM, NETHERLANDS; LEIDEN UNIV, LEIDEN, NETHERLANDS
CYA USA; COSTA RICA; NETHERLANDS

SO AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 1995) Vol. 57, No. 4, Supp. S, pp. 129.
ISSN: 0002-9297.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC No References

L17 ANSWER 31 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:476452 BIOSIS
DN PREV199598490752
TI Linkage disequilibrium analysis of **bipolar disorder** (**BP**) in the Costa Rican population.
AU **Escamilla, M. A. (1)**; **McInnes, L. A. (1)**; Spesny, M.; **Reus, V. I. (1)**; Shimayoshi, N. (1); Tyler, D. (1); Batki, S. (1); Vinogradov, S. (1); Meza, L.; Gallegos, A.; Molina, J.; Fournier, E.; **Leon, P.**; **Service, S. (1)**; Smith, L. (1); Silva, S.; **Sandkuijl, L.**; **Freimer, N. B.**
CS (1) Univ. California at San Francisco, San Francisco, CA USA
SO American Journal of Human Genetics, (1995) Vol. 57, No. 4 SUPPL., pp. A27.
Meeting Info.: 45th Annual Meeting of the American Society of Human Genetics Minneapolis, Minnesota, USA October 24-28, 1995
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 32 OF 50 MEDLINE DUPLICATE 13
AN 95243279 MEDLINE
DN 95243279
TI Linkage analysis of bipolar illness with X-chromosome DNA markers: a susceptibility gene in Xq27-q28 cannot be excluded.
AU De bruyn A; Raeymaekers P; Mendelbaum K; **Sandkuijl L A**; Raes G; Delvenne V; Hirsch D; Staner L; Mendlewicz J; Van Broeckhoven C
CS Department of Biochemistry, Born Bunge Foundation, University of Antwerp (UIA), Belgium..
SO AMERICAN JOURNAL OF MEDICAL GENETICS, (1994 Dec 15) 54 (4) 411-9.
Journal code: 3L4. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
AB Transmission studies have supported the presence of a susceptibility gene for **bipolar** (**BP**) illness on the X-chromosome. Initial linkage studies with color blindness (CB), glucose-6-phosphate dehydrogenase (G6PD) deficiency, and the blood

coagulation factor IX (F9) have suggested that a gene for **BP** illness is located in the Xq27-q28 region. We tested linkage with several DNA markers located in Xq27-q28 in 2 families, MAD3 and MAD4, that previously were linked to F9 and 7 newly ascertained families of **BP** probands. Linkage was also examined with the gene encoding the alpha 3 subunit of the gamma-amino butyric acid receptor (GABRA3), a candidate gene for **BP** illness located in this region. The genetic data were analyzed with the LOD score method using age-dependent penetrance of an autosomal dominant **disease** gene and narrow and broad clinical models. In MAD3 and MAD4 the multipoint LOD score data suggested a localization of a **BPI** gene again near F9. In the 7 new families the overall linkage data excluded the Xq27-q28 region. However, if the families were grouped according to their proband's phenotype **BPI** or BPII, a susceptibility gene for **BPI disorder** at the DXS52-F8 cluster could not be excluded.

L17 ANSWER 33 OF 50 MEDLINE DUPLICATE 14
AN 94091480 MEDLINE
DN 94091480
TI Nonlinkage of bipolar illness to tyrosine hydroxylase, tyrosinase, and D2 and D4 dopamine receptor genes on chromosome 11.
AU De bruyn A; Mendelbaum K; **Sandkuijl L A**; Delvenne V; Hirsch D; Staner L; Mendlewicz J; Van Broeckhoven C
CS Born Bunge Foundation, Department of Biochemistry, University of Antwerp, Belgium.
SO AMERICAN JOURNAL OF PSYCHIATRY, (1994 Jan) 151 (1) 102-6. Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199403
AB OBJECTIVE: Previous linkage and allelic association studies using DNA polymorphisms, cosegregation of cytogenetic abnormalities with psychiatric illness, and assignment of genes involved in neutotransmitter metabolism suggested that chromosome 11 may harbor a gene predisposing to bipolar illness. The authors examined linkage in the families of 14 probands with bipolar illness, with the candidate genes tyrosine hydroxylase (TH), D4 dopamine receptor (DRD4) at 11p15, tyrosinase (TYR) at 11q14-q21, and D2 dopamine receptor (DRD2) at 11q22-q23, as well as with the c-Harvey-ras oncogene (HRAS) and insulin gene (INS), both located at 11p15, a region that previously showed linkage to bipolar illness. METHOD: The genetic data were analyzed with both lod score analysis (parametric) and affected-sib-pair analysis (nonparametric); both narrow and broad definitions of the clinical phenotype were used. Further influences of diagnostic uncertainties were accounted for by using diagnostic probability classes weighing the stability of each

phenotype. RESULTS: Two-point linkage results excluded close linkage of bipolar illness to each candidate gene; negative results were also obtained when the narrow definition of the clinical phenotype was used. Moreover, multipoint linkage analysis of HRAS and INS excluded the 11p15 region encompassing both DRD4 and TH. In agreement with the negative linkage results, affected-sib-pair analysis did not show preferential sharing of marker alleles at any of the candidate genes. CONCLUSIONS: The negative results obtained under different genetic models exclude a frequent role for DRD4, TH, TYR, and DRD2 in the pathogenesis of bipolar illness.

L17 ANSWER 34 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 93:569255 SCISEARCH
GA The Genuine Article (R) Number: LW335
TI SEARCH FOR GENES PREDISPOSING TO **BIPOLAR DISORDER** USING MICROSATELLITES AND VAPSES
AU DEBRUYN A (Reprint); **SANDKUIJL L A**; RAES G; MENDELBAUM K; SOUERY D; MENDLEWICZ J; VANBROECKHOVEN C
CS UNIV INSTELLING ANTWERP, BORN BUNGE FDN, NEUROGENET LAB, B-2610 WILRIJK, BELGIUM; DIJKZIGT ACAD HOSP, DEPT CLIN GENET, ROTTERDAM, NETHERLANDS; FREE UNIV BRUSSELS, ERASME HOSP, DEPT PSYCHIAT, B-1050 BRUSSELS, BELGIUM
CYA BELGIUM; NETHERLANDS
SO AMERICAN JOURNAL OF HUMAN GENETICS, (SEP 1993) Vol. 53, No. 3, Supp. S, pp. 990.
ISSN: 0002-9297.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC No References

L17 ANSWER 35 OF 50 MEDLINE DUPLICATE 15
AN 93258405 MEDLINE
DN 93258405
TI Diminished support for linkage between manic depressive illness and X-chromosome markers in three Israeli pedigrees [see comments].
CM Comment in: Nat Genet 1993 Jan;3(1):4-5
Comment in: Nat Genet 1994 Mar;6(3):224
AU Baron M; **Freimer N F**; Risch N; Lerer B; Alexander J R; Straub R E; Asokan S; Das K; Peterson A; Amos J; et al
CS New York State Psychiatric Institute, Columbia University College of Physicians and Surgeons, New York 10032..
SO NATURE GENETICS, (1993 Jan) 3 (1) 49-55.
Journal code: BRO. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199308

AB The hypothesis that chromosomal region Xq27-28 harbours a gene for manic-depression has been a focus of interest in human genetics. X-linked inheritance of manic depressive illness has been re-examined in 3 multigeneration Israeli kindreds. Extension and re-evaluation of pedigree data, including new individuals, diagnostic follow-up, and analysis with DNA markers, shows greatly diminished support for linkage to Xq28. The peak lod scores in two of the pedigrees have dropped several lod units to clearly negative values at the RCP-F8-G6PD gene cluster. On the other hand, positive lod scores (Zmax = 2.09) are sustained in another pedigree at the same map location. None of the pedigrees show linkage to more proximal markers, including the Xq27 locus DXS98. Our analysis underscores the uncertainties in studying complex disorders.

L17 ANSWER 36 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:46001 BIOSIS
DN PREV199344022851
TI Genetic studies of manic depressive illness using large Central American pedigrees.
AU Freimer, N. (1); **Reus, V. (1); Sandkuijl, L. A.**; Spesny, M.; Peterson, A. (1); Rojas, E.; **Escamilla, M. (1)** ; Di Rienzo, A. (1); Gallegos, A.; **Leon, P.**
CS (1) Univ. Calif., San Francisco, Calif
SO American Journal of Human Genetics, (1992) Vol. 51, No. 4 SUPPL., pp. A187.
Meeting Info.: 42nd Annual Meeting of the American Society of Human Genetics, San Francisco, California, USA, November 9-13, 1992. AM J HUM GENET
ISSN: 0002-9297.
DT Conference
LA English

L17 ANSWER 37 OF 50 MEDLINE
AN 89220556 MEDLINE
DN 89220556
TI Behavioral aspects of thyroid disease in women.
AU **Reus V I**
CS Department of Psychiatry, Langley Porter Neuropsychiatric Institute, University of California School of Medicine, San Francisco.
SO PSYCHIATRIC CLINICS OF NORTH AMERICA, (1989 Mar) 12 (1) 153-65.
Ref: 121
Journal code: PBN. ISSN: 0193-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198908

AB Disturbances in thyroid regulation occur much more commonly in the female population and are not infrequently associated with behavioral symptomatology. Recognition of such gender differences in associational risk is important, for it may alter the clinical algorithm of assessment techniques and treatment interventions. From a scientific standpoint, interpretation of existing data and design of future studies exploring the relationship between thyroid regulation and behavior is likely to be improved if such sex differences are more commonly recognized and addressed.

L17 ANSWER 38 OF 50 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 88:69014 SCISEARCH
GA The Genuine Article (R) Number: L8448
TI **BIPOLAR DISORDER** IN A 6-YEAR-OLD BOY - A DIAGNOSIS BY PROXY
AU JEMERIN J M (Reprint); ROEBUCK K; PHILIPS I; WIENER J M; **REUS V**; ZEGANS L S
CS UNIV CALIF SAN FRANCISCO, LANGLEY PORTER NEUROPSYCHIAT INST, SCH MED, CHILDRENS INPATIENT UNIT, SAN FRANCISCO, CA, 94143 (Reprint)
CYA USA
SO JOURNAL OF THE AMERICAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY, (1988) Vol. 27, No. 1, pp. 133-137.
DT Discussion; Journal
FS SOCSEARCH
LA ENGLISH
REC Reference Count: 16

L17 ANSWER 39 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1987:475452 BIOSIS
DN BR33:113593
TI BASAL TSH BY IMMUNORADIOMETRIC ASSAY PREDICTS RESPONSE TO TRH.
AU **REUS V I**; **FREIMER N**; WOLKOWITZ O; PEEKE H V S
CS DEP. PSYCHIATRY, UCSF SCH. MED., 401 PARNASSUS AVE., SAN FRANCISCO, CALIF. 94143.
SO XVIITH INTERNATIONAL CONGRESS OF THE INTERNATIONAL SOCIETY OF PSYCHONEUROENDOCRINOLOGY, CHAPEL HILL-DURHAM, NORTH CAROLINA, USA, JUNE 28-JULY 3, 1987. NEUROENDOCRINOL LETT. (1987) 9 (3), 206. CODEN: NLETDU. ISSN: 0172-780X.
DT Conference
FS BR; OLD
LA English

L17 ANSWER 40 OF 50 MEDLINE
AN 86168059 MEDLINE
DN 86168059
TI Prediction of lithium dose: a mathematical alternative to the test-dose method.
AU Zetin M; Garber D; De Antonio M; Schlegel A; Feureisen S; Fieve R; Jewett C; **Reus V**; Huey L Y

SO JOURNAL OF CLINICAL PSYCHIATRY, (1986 Apr) 47 (4) 175-8.
Journal code: HIC. ISSN: 0160-6689.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198607
AB A method of estimating the optimal dose of lithium is presented. The charts of 548 patients were reviewed to obtain data regarding the factors thought to affect the lithium dose, and an equation to estimate the dose was derived by stepwise multiple linear regression. The equation was also applied to 390 patients to determine the difference between the estimated and the actual dose; the mean difference was only 19 mg/day and the standard deviation was 325 mg/day. Lithium level, presence of a cyclic antidepressant, age, sex, and weight were found to be important variables for estimation of lithium dose.

L17 ANSWER 41 OF 50 MEDLINE
AN 85280681 MEDLINE
DN 85280681
TI Habituation and cortisol dysregulation in depression.
AU **Reus V I**; Peeke H V; Miner C
SO BIOLOGICAL PSYCHIATRY, (1985 Sep) 20 (9) 980-9.
Journal code: A3S. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198512
AB The relationship between hypothalamic-pituitary-adrenal (HPA) dysregulation and skin conductance measures of habituation, stimulus specificity, and dishabituation was investigated in psychiatric patients exhibiting depressed affect. As a group, depressed patients showed a relative failure to dishabituate when compared with control subjects. Nonsuppression of cortisol following dexamethasone was associated with decreased response specificity as reflected in direct response measures and baseline skin conductance level. The impairment of response specificity to a novel stimulus is consistent with previous studies demonstrating a role for cortisol in the regulation of selective attention processes.

L17 ANSWER 42 OF 50 MEDLINE
AN 86043248 MEDLINE
DN 86043248
TI Effects of carbamazepine on noradrenergic mechanisms in affectively ill patients.
AU Post R M; Rubinow D R; Uhde T W; Ballenger J C; Lake C R; Linnoila M; Jimerson D C; **Reus V**

SO PSYCHOPHARMACOLOGY, (1985) 87 (1) 59-63.
Journal code: QGI. ISSN: 0033-3158.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198602
AB Noradrenergic mechanisms have been postulated to account for the anticonvulsant and psychotropic effects of carbamazepine. In order to assess this possibility in man, cerebrospinal fluid (CSF) was obtained from affectively ill patients before and during treatment with carbamazepine (average duration 29 days) at doses averaging 860 mg/day, achieving blood levels of 8.86 micrograms/ml. Neither plasma nor CSF norepinephrine (NE) nor CSF 3-methoxy-4-hydroxy-phenylglycol (MHPG) was significantly altered by carbamazepine. Baseline medication-free values in 21 depressed patients were not predictive of the degree of subsequent clinical antidepressant response. CSF NE decreased in four manic patients treated with carbamazepine. The many effects of carbamazepine on noradrenergic mechanisms in animals are discussed in relationship to these first studies of carbamazepine in man.

L17 ANSWER 43 OF 50 MEDLINE DUPLICATE 16
AN 83201716 MEDLINE
DN 83201716
TI Lithium carbonate and L-tryptophan in the treatment of **bipolar** and schizoaffective **disorders.**
AU Brewerton T D; **Reus V I**
NC RR-05755 (NCRR)
SO AMERICAN JOURNAL OF PSYCHIATRY, (1983 Jun) 140 (6) 757-60.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198308
AB The authors review theoretical and clinical data supporting the hypothesis that L-tryptophan may potentiate the effects of lithium carbonate and report on a double-blind clinical comparison of lithium plus L-tryptophan and lithium plus placebo in 9 bipolar and 7 schizoaffective patients. Overall the combination of lithium and L-tryptophan resulted in significantly greater improvement. However, the results may have been confounded by the greater, although nonsignificant, doses of neuroleptics administered to the group receiving L-tryptophan. The authors discuss the interactions of lithium and L-trypotophan with the serotonin system.

L17 ANSWER 44 OF 50 MEDLINE

AN 82179794 MEDLINE
DN 82179794
TI The "atypical" clinical picture of adolescent mania.
AU Ballenger J C; **Reus V I**; Post R M
SO AMERICAN JOURNAL OF PSYCHIATRY, (1982 May) 139 (5) 602-6.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198208
AB The authors examined the records of 9 manic patients under age 21 and 12 over age 30 for the incidence of "schizophrenic" and manic symptoms. The adolescent patients had a higher incidence of each of the 10 schizophreniform symptoms rated and significantly more delusions and ideas of reference. Significantly more adolescent patients had 3 or more schizophreniform symptoms; they also had symptoms typical of mania. These findings highlight the diagnostic importance of affective symptoms in psychotic adolescents with mixed symptoms and raise important clinical and theoretical questions about the atypical clinical picture of manic-depressive illness in young patients.

L17 ANSWER 45 OF 50 MEDLINE
AN 81059946 MEDLINE
DN 81059946
TI Failure of naloxone to reduce manic symptoms.
AU Davis G C; Extein I; **Reus V I**; Hamilton W; Post R M; Goodwin F K; Bunney W **E** Jr
SO AMERICAN JOURNAL OF PSYCHIATRY, (1980 Dec) 137 (12) 1583-5.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198103
AB The authors conducted a double-blind placebo-controlled study in which patients with a wide range of manic symptoms were administered 20 mg of naloxone subcutaneously. Naloxone failed to improve manic severity, activation-arousal, or elation-grandiosity for intervals up to 3 hours. Global nurse ratings of mania did not improve over an 8-hour period. The authors suggest that the question of endorphin involvement in mania has not been resolved and recommend clinical studies with longer acting oral narcotic antagonists such as naltrexone.

L17 ANSWER 46 OF 50 MEDLINE
AN 79206945 MEDLINE
DN 79206945

TI Clinical implications of state-dependent learning.
AU **Reus V I**; Weingartner H; Post R M
SO AMERICAN JOURNAL OF PSYCHIATRY, (1979 Jul) 136 (7) 927-31.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197910
AB Researchers have found that state-dependent learning is associated with the administration of a wide variety of drugs. Recent data suggest that similar phenomena may occur secondary to endogenous changes in neuroregulatory substances. The authors point out that awareness of such changes in cognitive processing strategies and abilities should help to further our understanding of the phenomenology of psychiatric states and should generate psychotherapeutic techniques designed to maximize the transfer of information across psychiatric states.

L17 ANSWER 47 OF 50 MEDLINE
AN 79163209 MEDLINE
DN 79163209
TI Lithium-induced thyrotoxicosis.
AU **Reus V I**; Gold P; Post R
SO AMERICAN JOURNAL OF PSYCHIATRY, (1979 May) 136 (5) 724-5.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197908

L17 ANSWER 48 OF 50 MEDLINE
AN 80000759 MEDLINE
DN 80000759
TI d-Amphetamine: effects on memory in a depressed population.
AU **Reus V I**; Silberman E; Post R M; Weingartner H
SO BIOLOGICAL PSYCHIATRY, (1979 Apr) 14 (2) 345-56.
Journal code: A3S. ISSN: 0006-3223.
CY United States
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198001
AB The effect of intravenous d-amphetamine on memory functions in a group of depressed patients was examined in a double-blind placebo-controlled study. Active drug administration resulted in an

increase in verbal free recall but no change in cued recall, suggesting specific effects on memory processes. The level of psychological processing of the presented stimulus was shown to interact with drug-induced facilitation of recall. Improvement in memory of more shallowly processed material under amphetamine related significantly to subjects' base-line indices of noradrenergic function. Drug-induced changes in mood did not correlate with improvement in cognitive functioning. The interrelationships between biochemical determinants of mood and memory are discussed in light of these findings.

L17 ANSWER 49 OF 50 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 17
AN 1979:449645 CAPLUS
DN 91:49645
TI Effect of lithium carbonate on memory processes of bipolar affectively ill patients
AU **Reus, Victor I.**; Targum, Steven D.; Weingartner, Herbert; Post, Robert M.
CS Biol. Psychiatry Branch, Natl. Inst. Ment. Health, Bethesda, MD, 20014, USA
SO Psychopharmacology (Berlin) (1979), 63(1), 39-42
CODEN: PSCHDL; ISSN: 0033-3158
DT Journal
LA English
AB The effect of long-term Li2CO3 treatment on parameters of immediate, short-, and long-term memory was examd. in a group of bipolar affectively ill patients. The Li treatment group recalled significantly fewer words across trials on a verbal learning task than a group of bipolar affectively ill patients receiving no medication. The ability to consistently recall material for which prior learning had been demonstrated was also decreased and accounted for most of the variance in total no. of words recalled. Possible mechanisms of effect are discussed.

L17 ANSWER 50 OF 50 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1978:235396 BIOSIS
DN BA66:47893
TI VASOPRESSIN IN AFFECTIVE ILLNESS.
AU GOLD P W; GOODWIN F K; **REUS V I**
CS CLIN. PSYCHOBIOL. BRANCH, NATL. INST. MENT. HEALTH, 9000 ROCKVILLE PIKE, ROOM 4S239, BUILD. 10, BETHESDA, MD. 20014, USA.
SO LANCET, (1978) 1 (8076), 1233-1236.
CODEN: LANCAO. ISSN: 0023-7507.
FS BA; OLD
LA English
AB Animal studies [rats] have revealed 2 important aspects of vasopressin function which made this peptide a suitable candidate for involvement in complex behavioral syndromes: vasopressin deficiency produces deficits of behavior which are reversed by